Study of Occupational Asthma among Different Occupants in Dhaka and Prescribing Habit by Health Practitioners

A report submitted to the department of Pharmacy, East West University, Bangladesh, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

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Declaration by the Research Candidate

I, Yeashir Arafath Emon, hereby declare that the dissertation entitled "**Study of Occupational Asthma among Different Occupants in Dhaka and Prescribing Habit by Health Practitioners**" submitted by me to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the award of the degree of Bachelor of Pharmacy (Honors) is a bonfire record of original research work carried out by me during 2011-2012 under the supervision and guidance of Mr. Razibul Habib, lecturer, Dept. of Pharmacy, East West University and it has not formed the basis for the award of any other Degree/Diploma/Fellowship or other similar title to any candidate of any University.

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Date: 12 / 07 / 2012

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Certificate

This is to certify that the thesis "**Study of Occupational Asthma among Different Occupants in Dhaka**" submitted to the department of pharmacy, East West University in partial fulfillment of the requirements of the degree of Bachelor of Pharmacy was carried out by **Yeashir Arafath Emon (ID# 2006 – 1 – 70 – 017)** under our guidance and supervision and that no part of the thesis has been submitted for any other degree. We further certify that all the sources of information and laboratory facilities availed of in this connection is duly acknowledged.

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Acknowledgement

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ABSTRACT

Occupational Asthma is also called "**Work – related Asthma**" in which workers are regularly getting exposed by allergens existing in their working environment which leads them to a chronic allergic asthma. So, it is an irritant – induced asthma where the irritants are existing in the environment of occupation. High – level of exposure to such allergens can be fatal, since response will be immediate and cause permanent damage to the lung. This situation can be prevented by controlling the environment of working and screening out the employees who are susceptible or sensitive to such allergens. In Bangladesh, researches on Occupational Asthma are narrow. However, Immunoglobulin E – independent immunological or nonimmunological mechanisms alone are able in little to carry the cause of occupational asthma. So, a descriptive statistical study is being conducted to put forward a little portion of the big picture on the actual situation regarding occupational asthma in Bangladesh. Since most of the work – related asthmatic patients are of low-socio-economic status, further clinical studies are needed to measure the exposures that increase the knowledge about the influence of possible confounders of Occupational Asthma. In occupational asthma, the trigger is a substance or condition in the workplace that causes asthma symptoms. Most of these substances and conditions are very common and are not normally considered hazardous. Although these substances and conditions can be encountered in almost any workplace, occupational asthma is most common in workers in the following industries and jobs: Plastics industry, Rubber industry, Chemical industry, Textile industry, Electronics industry, Painting, Printing, Dyeing, Metalworking, Welding, Oil refining, Cleaning, Baking and food processing, Farming, Gardening, landscaping, horticulture, Working with animals, Laboratory work

Keywords: Asthma, Occupational Asthma, Symptoms of Asthma, Mechanism of Asthma, Irritant-induced Asthma, Reactive airways dysfunction syndrome (RADS), COPD

Chapter 1

INTRODUCTION

CHAPTER 1: INTRODUCTION

1.1 Introduction

'Asthma is defined as a chronic inflammatory disorder of the airways involving airflow limitation that is at least partly reversible and which results in recurrent episodes of symptoms such as wheezing, breathlessness, chest tightness, and cough', (Douwes, Pearce, & Heederik, 2002).

'The chronic inflammation causes an associated increase in airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning', (O'Bryan, 2012).

According to American Lung Association,

> It is a chronic lung disease characterized by reversible airway obstruction resulting from inflammation of the lung's airways and a tightening of the muscles around them. Some degree of airway obstruction is often constantly present in those with asthma, but more severe reactions can occur due to exposure to a variety of triggers, (Kramer & Chen, 2010).

The journal also said that 'Asthma triggers vary depending upon person and environment, but some known triggers include cigarette and other smoke, mold, pollen, dust, animal dander, exercise, cold air, household and industrial products, air pollutants, and infections', (Kramer & Chen, 2010).

Asthma is recognized as a condition with variable airway obstruction with pathophysiological features that include activation of a wide range of inflammatory and structural cells. Additionally, structural changes in the airways have been demonstrated. This includes increased thickening of components in the basement membrane region, increased smooth muscle mass, increased vascularization and many other events that is often referred to as remodeling of the airways. These processes and the underlying mechanisms have attracted considerable attention, (Sandström, 2010).

1.1.1 Anatomy of Asthma Attack

During an asthma episode, tightening of the smooth muscles around the bronchial tubes causes them to become inflamed, narrow inside, and produce excess mucus. This makes it difficult for air to pass in and out of the lungs and decreases the oxygen levels in the blood. A person suffering from an asthma attack has a sensation similar to drowning.

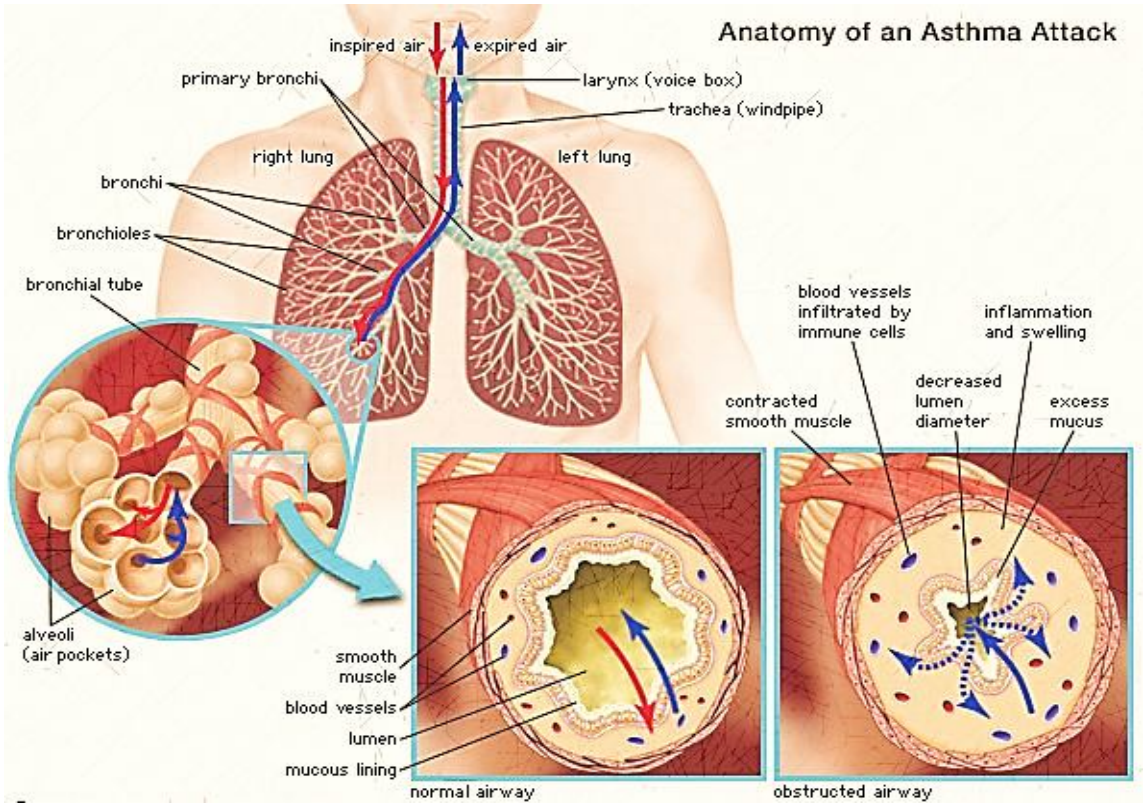


Figure 1: Anatomy of Asthma Attack showing obstructed air way

'When the respiratory system is working properly, the air we breathe passes in and out of the lungs through a network of airways. But for people with asthma, even a minor irritant will set off an immune response that can shut down the airways, (Taylor, 2012).

Irreversible airflow limitation in subjects with a previously clear history of asthma and absence of smoking is commonly considered as fixed airway obstruction because of remodeling changes of the airways. Increased stiffness and reduced compliance of the airway wall has been associated with enhanced matrix deposition that may be protective against excessive bronchoconstriction. On the other hand, an irreversible airway narrowing may just as well be an adverse reaction for the patient, who loses respiratory

capacity. In very severe asthma, disruption of alveolar walls attaching to bronchi may occur and thereby adding to airway narrowing, (Sandström, 2010).

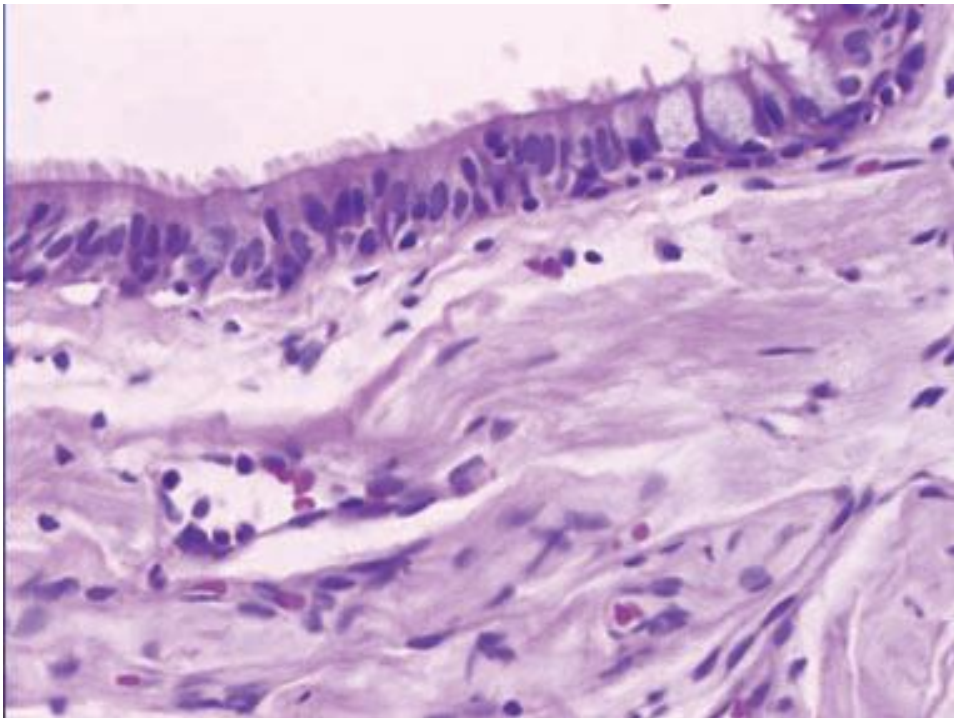


Figure 2: Bronchial mucosa in asthmatic subject with widespread structural changes associated with airway remodeling

1.1.2 Occupational Asthma and Chronic Obstructive Pulmonary Disease (COPD)

In diseases such Occupational Asthma and Chronic Obstructive Pulmonary Disease (COPD), the occurrence of lung hyperinflation may provide a stronger stimulation of SARs and evokes greater reflex effects. Hyperinflation is followed by an increase of expiratory muscle activity and changes in pattern of breathing, both serving as compensatory mechanisms, (Baroffio, Barisione, Crimi, & Brusasco, 2009).

In addition, mechanoreceptors may be involved in the deep breath-induced relief of breathlessness due to airway narrowing. This is consistent with the common experience that a sigh and/or a deep inspiration may attenuate the shortness of breath. In asthma, the bronchodilator efficacy of deep breaths is blunted.

The contribution of neural dysfunction to this phenomenon is not completely understood and needs further investigation. The peripheral afferent signals from sensory nerve endings reaching the vagal nuclei are centrally integrated and the degree of basal autonomic nerve activity in the airways is closely associated with respiratory drive, suggesting that ASM activity is neurally regulated to facilitate an efficient gas exchange.

A new investigative field concerning the pathogenesis of AHR is the possible neural alteration associated with airway wall remodeling in Occupational asthma and COPD. For example, it has been shown that in asthmatic subjects an altered neural regulation may be due to an increased expression of nerve growth factor (NGF) or neurotrophins. The NGF is produced by ASM, epithelial cells and inflammatory cells and its circulating level is related to asthma severity. On the other hand, neurotrophins activate not only the tropomyosin-related kinase A receptor and the receptor p75 for neurotrophins, but also pathways promoting cell survival through the transcription nuclear factor-kappaB, (Baroffio, Barisione, Crimi, & Brusasco, 2009).

Readmission following hospital admission for chronic obstructive pulmonary disease (AECOPD) is common, occurring at least once in 60% of patients within 1-year of discharge. Furthermore, rapid readmission within 3-months of discharge affect 30% of patients with AECOPD, and underscores the fact that approximately one third of

exacerbations are recurrent events occurring within 8 weeks of an initial exacerbation. In Europe, early discharge services (EDS) are increasingly the candidate care model to cost-effectively and safely manage patients with AECOPD at home. These services, which can care for 30% of patients admitted for AECOPD, include admission prevention in accident and emergency, rapid discharge (< 48 hours), assisted discharge (≥ 2 days after admission), and nurse led support in patients' homes. However, evidence that EDS reduce readmission rates for AECOPD is equivocal. In a before and after study of early discharge care followed by rapid-access out-patient support, patients admitted for AECOPD had significantly fewer admissions 6 and 12 months after participation in the programme. Similarly, in a Spanish study of patients with severe COPD, the provision of an assisted discharge and exacerbation prevention programme reduced readmission rates from 35% to 17%, (Coventry, Gemmell, & Todd, 2011).

1.1.3Mechanism of Asthma: An Inflammatory Response

'Asthma has been defined as having three phenotypic characteristics: intermittent and reversible airway obstruction; increased airway responsiveness to contractile stimuli; and airway inflammation. Pulmonary inflammation is a hallmark of asthma and is directly related to asthma severity as a function', (Delfino, 2002).

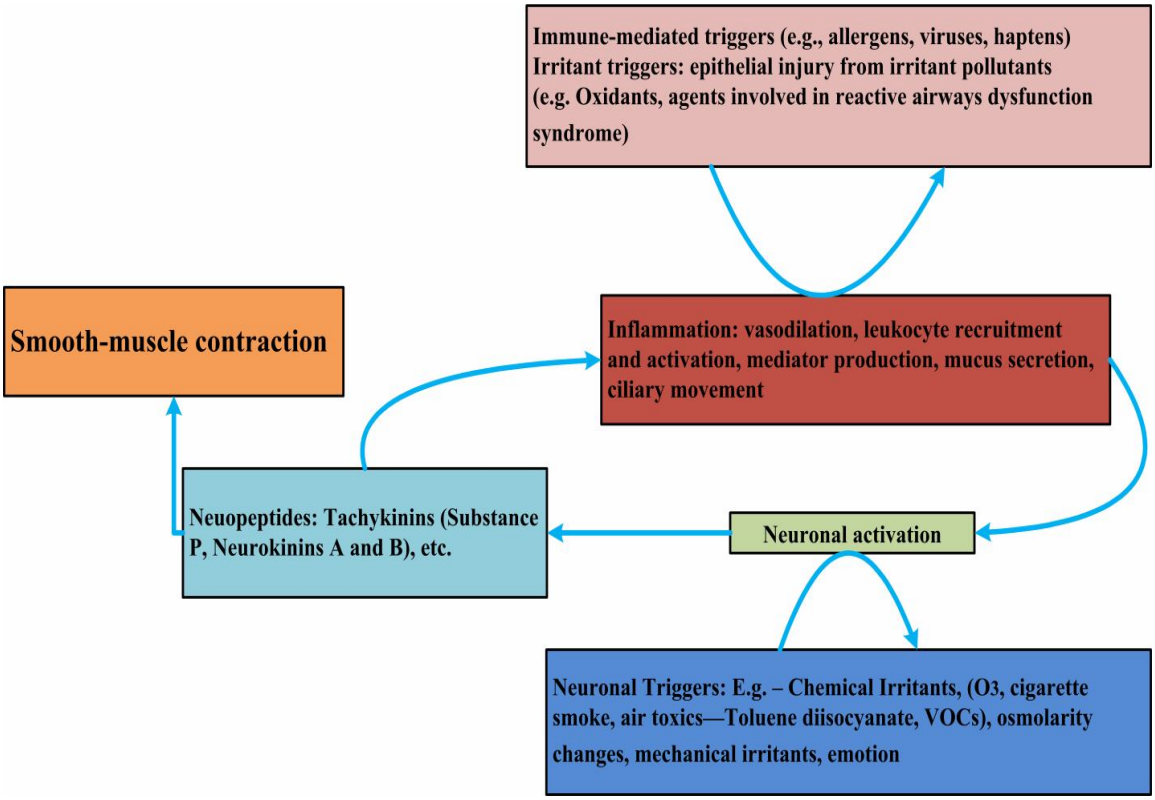


Figure 3: Hypothetical feedback loop between inflammatory processes and neuronal processes that trigger Inflammation

Three general mechanisms of inflammation in asthma include –

1. Immunoglobulin E (IgE) mediated Inflammation
2. Neurogenic induced Inflammation
3. Irritant induced Inflammation

1.1.3.1 Immunoglobulin E (IgE) mediated Asthma

'The principal inflammatory mechanism in asthma is an **IgE-Mediated Reaction** whereby an antigen cross-links with an IgE antibody specific to that antigen on the surface of mast cells and other immune cells', (Delfino, 2002).

Delfino also said that 'Low molecular weight agents involved in IgE-mediated reactions, including certain air toxics, act as Haptens which ….must first react with endogenous or exogenous proteins to form a complete antigen (e.g., formaldehyde-albumin). IgE-mediated mechanisms are key in early-phase asthmatic reactions (within minutes)', (Delfino, 2002).

According to Mitsunobu, et al (2000), IgE mediated asthma is also called Atopic Asthma,

> ….which is clinically evaluated according to serum IgE levels, skin reactivity, radioallergosorbent test score to inhalant allergens and bronchial challenge with corresponding allergens. Patients with atopic asthma often have a family history of allergic diseases suggesting that IgE –mediated allergy is closely related to family history of allergic diseases. It is generally believed that true allergic asthma very seldom begins in elderly patients and that when it does occur, it is actually intrinsic asthma', (Mitsunobu, et al., 2000).

IgE Mediated Asthma can also be termed as **Allergic Asthma** as petitioned by Roger G. Walker of **MD Bioproducts** that 'it is the most common form of asthma. In allergic asthma, the body initiates an immune response to an allergen such as pet dander, dust-mites, mold or pollen that results in IgE antibodies. This process is commonly referred to as allergic sensitization', (Roger, 2012).

The author also explained the possible mechanism that,

Most allergens are proteins (can be a carbohydrate or lipid) that pass through the epithelial barrier and come into contact with a dendritic cell. The dendritic cell presents the antigen peptide to Naïve T cells in the context of major histocompatibility complex (MHC) class II molecules. This is recognized by a Naïve T cell that can become an allergen-specific T helper-2cells that will secrete the cytokines IL-4 and IL-13 necessary for the activation of B cells to produce IgE antibodies. Circulating IgE antibodies attach to the surface of mast cells and basophiles via its high affinity receptor for IgE and/or continue to re-circulate throughout the body. Subsequent exposure to the same allergen will cause cross-linking of the cell-bound antigen specific IgE, which causes degranulation and the release of mediators resulting in IgE – mediated Asthma, (Roger, 2012).

Allergic Asthma consisted of the following criteria or characteristics:

(1) Initiation of asthma caused by exposure in the workplace to a sensitizing agent known to cause allergic-type asthma; (2) Cases of asthma occurring after a latent period of exposure lasting at least 4 months; and (3) cases with a consistent temporal relationship between attacks of asthma and workplace exposures, (Brooks, Hammad, Richards, Giovinco-Barbas, & Jenkins, 1998).

1.1.3.2 Neurogenic Asthma

‘Neurogenic inflammation involves a spread of the inflammatory response via the release of neurotransmitters or activation of afferent nerves by the action of inflammatory mediators. Inflammatory mediators can trigger the activation of noradrenergic,

noncholinergic nerves to release tachykinins. A cascade of bronchoconstrictive reflexes and of inflammatory events can follow', (Delfino, 2002).

The release of neurotransmitters may exacerbate the inflammatory response in Asthma. Such neurogenic inflammation has been documented in a number of inflammatory diseases. Neurogenic inflammation due to release of neuropeptides from sensory nerves in airways may contribute to the inflammatory response in asthmatic airways.

> Tachykinins (substance P and neurokinin A) released from airway sensory nerves may cause bronchoconstriction, vasodilatation, plasma exudation, and mucus secretion, whereas another sensory neuropeptide, calcitonin generated peptide, may contribute to hyperemia of inflammation. Airway epithelial damage in asthma exposes sensory nerves which may become sensitized by inflammatory products (including prostaglandins and cytokines) so that neuropeptides are released via a local reflex trigger such as bradykinin, resulting in exaggerated inflammation. The effects of tachykinins may be amplified further by loss of the major degrading enzyme, neutral endopeptidase, from epithelial cells, (Barnes, 1992).

1.1.3.3 Irritant induced Asthma

'Irritant-induced asthma (or IIA for short) is a type of asthma caused by exposure to gas, fumes, vapors or inhaled particles. A similar condition is Reactive airway dysfunction syndrome (or RADS for short)', (Loengard, 2008)

> Reactive airways dysfunction syndrome (RADS) is a primary example of a type of asthma where toxic irritant-induced inflammation is a key mechanism. 'RADS' has been identified in occupational settings and is defined as an **Irritant-Induced Nonimmunologic Asthma** with no latency period. It is nonimmunologic in the sense that bronchial epithelial injury is the primary causal event and typical phases of the immune response are absent. It is an example of an inflammatory mechanism of air toxics, (Delfino, 2002).

The writer of the article from the previous citation also stated that 'Both IIA and RADS are classified as **Occupational Asthma**, because many of the exposures to irritant substances that lead to RADS and IIA occur in the workplace. RADS and IIA were first recognized as distinct illnesses in 1985', (Loengard, 2008).

Criterias for asthma to be determined as an Irritant-induced asthma are the following:

> (1) Initiation of asthma was temporally related to an irritant exposure; (2) Asthma symptoms developed during the time period that an irritant exposure was taking place; (3) Exposures is either intermittent or continuous in nature; and (4) Subjects were excluded if the irritant exposure lasted more than 16 weeks (4 months) before initiation of asthma, (Brooks, Hammad, Richards, Giovinco-Barbas, & Jenkins, 1998).

Table 1: Irritants causing Irritant –Induced Asthma and RADS, (Brooks, Hammad, Richards, Giovinco-Barbas, & Jenkins, 1998)

Irritant Responsible for Irritant Induced Asthma and RADS
Pesticide Spraying
Cement Sealant
Mixed Solvent Vapors And Mist

Table 2: Irritants causing Irritant –Induced Asthma and RADS, (Brooks, Hammad, Richards, Giovinco-Barbas, & Jenkins, 1998)

Irritant Responsible for Irritant Induced Asthma and RADS
Household Bleach Vapors
Spray Paint
Sulfur Dioxide Gas
Titanium Tetrachloride Mist
Volatile Organic Vapors from Poor Indoor Air Quality
Ammonia Vapors
Muriatic Acid Spill
Welding Fumes
Chlorine Gas
Burned Freon Fumes
Fire Retardant Aerosol
Caustic Soda Aerosol
Diphenylmethane diisocyanate

Hexamethylene diisocyanate
Toluene diisocyanate
Flour dust
Acrylates-methacrylate ester
Acrylates-cyanoacrylate ester

1.2 Occupational Asthma

'Airflow limitation and airway hyperresponsiveness caused by exposure to a workplace environment, and no other environments, defines the disease of Occupational Asthma', (Namath & Kuschner, 2006).

'Occupational asthma is an occupational condition defined 'A disease characterized by variable airflow limitation and/or airway hyper-responsiveness due to causes and conditions attributable to a particular occupational environment and not stimuli encountered outside the workplace', (Haggstrom, 2012).

'Work-related asthma is the most commonly reported occupational lung disease…..Occupational exposures can trigger asthma exacerbations in asthmatic workers or induce asthma in a previously healthy worker', (Bonauto, Curwick, Brodkin, Beckett, & Shusterman, 2006).

Another definition says that,

> Occupational asthma is a breathing (respiratory) disease caused by exposure to a trigger in the workplace. A trigger is an external factor or condition in the body that causes the asthma to occur or worsen. The list of known triggers is long and varied. The trigger generally is something inhaled. Occupational asthma can occur

in almost any line of work or any work environment, including offices, stores, hospitals, and medical facilities, (Schiffman, 2010).

1.2.1 Asthmatic Triggers and their Occupation of Exposure

Triggers of Occupational Asthma include contaminants in the air, such as smoke, chemicals, vapors (gases), fumes, dust, or other particles; allergens in the air, such as molds, animal dander, and pollen.

Early recognition and avoidance of the asthma trigger is particularly important in occupational asthma. Because people spend so much time at work, they tend to have extensive exposure to their trigger by the time the cause of the symptoms is recognized as Occupational asthma. It is the most common work-related lung disease in developed countries, (Schiffman, 2010).

These triggers are also called, 'Respiratory Sensitizers or Asthmagens. They can cause a change in people's airways and lungs, known as the Hypersensitive State. Once the lungs become hypersensitive, further exposure to the substance, even at quite low levels, may trigger an asthmatic attack', (Gale, 2011).

Bonauto, et al (2006) has determined several asthmatic triggers and their occupation of exposure,

Table 3: Asthmatic Triggers and their Occupation of Exposure (Bonauto, Curwick, Brodkin, Beckett, & Shusterman, 2006)

Asthmatic Triggers	Occupation of Exposure

Asthmatic Triggers	Occupation of Exposure
Animals	
Animal Urine and Proteins	Animal Handlers in Laboratories, Research Scientists
Grain Mite	Farmers, Grain-Store Workers
Prawns, Crabs	Seafood Processors
Egg Protein	Egg Producers
Plants	
Grain Dust	Grain Storage Workers
Wheat Flour, Rye Soy	Bakers, Millers
Latex	Health – Care Workers
Henna, Gum Acacia	Hairdressers, Printers

Table 4: Asthmatic Triggers and their Occupation of Exposure (Bonauto, Curwick, Brodkin, Beckett, & Shusterman, 2006)

Asthmatic Triggers	Occupation of Exposure
Enzymes	
Derived/Proteases From *Bacillus Subtilis*	Detergent Industry Workers
Pancreatin, Papain, Pepsin	Pharmaceutical And Food Industry Workers
Fungal Amylase	Bakers
Wood Dusts Or Barks	
Cinnamon, Oak, Mahogany	Sawmill Workers, Carpenters
Chemicals	
Diisocyanates	Plastics, Varnish, Packing and Shipping Workers

Phthalic/Acid Anhydride	Plastic and Resin Workers
Ethylene Diamine/Complex Amines	Photography and Shellac Workers
Azodicarbonamide	Plastics and Rubber Workers
Reactive Dyes	Dyeing and Textile Workers
Methyl Methacrylate	Health – Care Workers
Institutional Cleaning Agents	Janitorial Staff
Drugs	
Penicillins, Methyldopa, Cimetidine	Pharmaceutical and Health – Care Workers
Metals	
Halogenated Platinum Salts	Platinum – Refining Workers
Cobalt	Metal Grinders
Chromium, Nickel	Metal – Plating Workers

1.2.2 Symptoms of Occupational Asthma

The symptoms of Occupational Asthma may develop immediately after exposure, but sometimes may only appear after several hours' exposure. Whilst it may not necessarily be occupational asthma, the evidence indicates that the diagnosis is likely to be occupational asthma in about half the cases referred to a chest physician. When any one worker develops confirmed occupational asthma, the exposure and presence of symptoms of other workers should be investigated.

'In most people with occupational asthma, the symptoms appear a short time after beginning work and subside after leaving work. Many have no symptoms or milder symptoms on days they do not work. The symptoms return when they return to work', (Schiffman, 2010).

The Author also said,

In some, the symptoms worsen gradually over the work week, go away over the weekend, and return when the new work week starts. In others, the symptoms are slow to develop and may not be noticed until after leaving work for the day. In the later stages of the disease, after long-term regular exposure, symptoms may not go away even after leaving the workplace, (Schiffman, 2010).

The followings are the most common symptoms of occupational asthma (Most people do not have all these symptoms):

1. Coughing
2. Wheezing
3. Chest tightness
4. Chest pain
5. Prolonged shortness of breath
6. Extreme fatigue

Allergy symptoms that occur at work but get better away from work also may be a sign of irritants in the air that could provoke asthma symptoms. The following symptoms could occur:

1. Eyes: itchy, burning, or watery
2. Nose: itchy or stuffy, sneezing
3. Skin: itchy, red, or irritated

Workers should report the following symptoms as soon as they develop, to health-care Personnel such as attacks of wheezing, coughing, chest tightness, sneezing, runny nose and Conjunctivitis (itchy and inflamed eyes) are other key symptoms, (Bento, 2010, p. no. 4).

Table 5: Symptoms of Occupational Asthma according to Severity

Early Signs	Mild and Moderate Attacks	Severe Attacks
Wheezing	Coughing up mucus	Inability to breath
Breathlessness	Increased tightness in chest	Trouble talking
Tightness in the chest	*	Muscles in neck tighten
Coughing	*	Bluish or grayish color to lips and fingernails

1.2.3 Outcome of Occupational Asthma

According to Moira Chan-Yeung (1995),

> Many follow-up studies of patients with occupational asthma due to various agents have shown that the majority failed to recover even after years of removal from exposure. Since these patients did not have asthma before employment and they had a specific reaction to the offending agent, one can only assume that the persistence of symptoms is due to previous occupational exposure. This finding suggests that once an individual develops asthma from any stimulus, self-perpetuating processes may be responsible for the chronic inflammation in the airways resulting in persistence of nonspecific bronchial hyperresponsiveness and asthma symptoms, (Chan-Yeung, 1995).

So, effects excessive exposure to occupational irritants may pursue the patient forever in his / her entire lifetime with Occupational Asthma.

1.2.4Determinants for Development of Occupational Asthma

The development of occupational asthma is dependent on Exposure Factors, Predisposing Host Factors, Genetic Factors and Cofactors.

1.2.4.1 Exposure Factors

Studies show that the higher is the exposure, the higher the prevalence of occupational asthma.

> Once a subject is sensitized to an occupational agent, he or she is likely to develop bronchoconstriction at a much lower concentration than the level that led to sensitization. Intermittent high exposure may be more important in inducing asthma; many new cases of occupational asthma occurred after exposure to a spill of the chemical, (Chan-Yeung, 1995, p. no. 250).

Occupational exposure to complex platinum salts is a well-known cause of occupational asthma. Although there is evidence that platinum refinery workers may also be sensitized to other precious metals, such as palladium or rhodium, no instances of occupational asthma due to an isolated sensitization to palladium have been reported. A case is reported of occupational rhinoconjunctivitis and asthma in a previously healthy worker exposed to the fumes of an electroplating bath containing palladium. There was no exposure to platinum. Sensitization to palladium was documented by skin-prick tests. The skin-prick test was positive with $Pd(NH_3)_4Cl_2$, but not with $(NH_4)_2PdCl_4$. Corresponding salts of platinum were all negative. A bronchial provocation test with $Pd(NH_3)_4Cl_2$ (0.0001% for a total of 315 s, followed by 0.001% for a total of 210 s) led to an early decrease in forced expiratory volume in one second (-35%). A similar exposure

(0.001% for a total of 16 min) in an unrelated asthmatic gave no reaction. This case shows that an isolated sensitization to palladium can occur and that respiratory exposure to palladium is a novel cause of metal-induced occupational asthma, (Daenen, Rogiers, Van de Walle, Rochette, Demedts, & Nemery, 1993).

Agriculture is associated with a high risk of development of occupational asthma. The best treatment would be complete avoidance of exposure, which would often imply a change of occupation. For a variety of reasons, including economic factors, this approach is rarely feasible. As a consequence, education about technical, organizational and personal preventive measures is an important part of disease management, particularly since educational interventions are generally known to be effective in asthma treatment. An important biomarker of asthma is exhaled nitric oxide fraction (FeNO), which is known to be sensitive to allergen burden as well as anti-inflammatory therapy. Changes in FeNO, after either allergen exposure or corticosteroid treatment, occur rapidly and are detectable after a short time. It was thus hypothesized that FeNO might be suitable for the detection of a reduction in airway inflammation within a few weeks after an educational intervention in farmers with occupational asthma, in parallel to a change in respiratory symptoms, (Dressel, Gross, De la Motte, Su¨ltz, Jo¨rres, & Nowak, 2007).

1.2.4.2 Predisposing Host Factors

Predisposing host factors are different for –

1. IgE-dependent Occupational Asthma

2. Non-IgE-dependent Occupational Asthma

1.2.4.2.1 Predisposing Host Factors for IgE-dependent Occupational Asthma

Atopy and smoking are important host determinants for agents that induce asthma through an IgE-dependent mechanism. The majority of patients with IgE dependent occupational asthma are atopic subjects. Smoking has been found to be an important determinant for sensitization.

For Example, ‘A prospective study of platinum refinery workers has shown that about 70 to 80% of smokers were sensitized to platinum salt after a period of 4 to 5 years as opposed to less than half of the nonsmokers’, (Chan-Yeung, 1995).

Another example, ‘A study of workers exposed to tetrachlorophthalate anhydride has demonstrated that atopic smokers had higher prevalence of sensitization than atopic subjects alone, indicating that there is interaction between atopy and smoking’, (Chan-Yeung, 1995).

1.2.4.2.2 Predisposing Host Factors for Non-IgE-dependent Occupational Asthma

Both atopy and smoking are not important predisposing host factors for agents that induce asthma through non-IgE-dependent mechanisms. In this case, the majorities of patients is non-atopic subjects and are nonsmokers. Thus far, no predisposing host factors have been identified for these types of occupational asthma.

1.2.4.3 Genetic Factors

Asthma and allergies are good models for studying complex diseases resulting from the interaction of genetic and environmental factors, and Occupational Asthma (OA) is a good model for such studies.

This is applicable for Occupational Asthma with a latency period which includes the following factors:

1. Human Leukocyte Antigen System

2. Oxidative Stress

1.2.4.3.1 Human Leukocyte Antigen System

Most reported genetic studies of Occupational Asthma have investigated the importance of human leukocyte antigen (HLA) class-II polymorphisms in increasing or decreasing the risk of developing sensitization and Occupational Asthma.

HLA class-II molecules are highly polymorphic and are therefore plausible candidate genes that influence the development of a specific immunological response. HLA association with Occupational Asthma has been shown in workers exposed to low molecular weight chemicals, including acid anhydrides, isocyanates, platinum salts, (Mapp, 2003).

1.2.4.3.2 Oxidative stress

Some important chemical sensitizers, such as isocyanates, may cause oxidative stress at the epithelial surface when they form conjugates with human proteins.

Isocyanates exposure induces intracellular hydrogen peroxide production and intercellular adhesion molecule (ICAM)-1 expression on cultured mononuclear cells, suggesting that the production of reactive oxygen species by monocytes at the site of exposure of an isocyanate may contribute to tissue damage. Therefore, defects in

antioxidant defenses could contribute to the susceptibility of isocyanate-induced asthma.(Mapp, 2003).

> Genetics has a significant influence on Occupational Asthma, but the relationship of genetic susceptibility and gene-environment interactions has not yet been established. Rapid advances in several fields, especially in molecular biology and statistical analysis, have allowed the increased understanding of the development of these diseases, but a clear picture of the mechanisms that lead to asthma onset and persistence is still lacking, (Mapp, 2003).

1.2.4.4 Co-factors

Although most patients with occupational asthma develop symptoms within 2 years of onset of exposure, some individuals developed the disease many years later. However, there is no information about factors that initiate the onset of sensitization or onset of symptoms.

For example, 'Many patients with occupational asthma gave a history that described a persistent cold at the onset of symptoms that failed to clear. It is difficult to know whether the symptoms are due to a viral infection or are symptoms of the allergic processes', (Chan-Yeung, 1995).

1.2.5 Treatment for Occupational Asthma

1.2.5.1 Treatment of Occupational Asthma by Medication

Medications for Occupational Asthma are similar to those for regular asthma. These are categorized into two general classes –

1. Long – term control medications
2. Quick – relief medications

1.2.5.1.1 Long – term control medications

Long-term control medications are used to achieve and maintain control of persistent asthma and quick-relief medications used to treat acute symptoms and exacerbations.

The Medications included are –

1. Inhaled Corticosteroids (E.g. – Beclomethasone, Fluticasone)
2. Cromoglycate (E.g. – Sodium cromoglycate, Nedocromil Sodium and Ketotifen)
3. Immunomodulators (E.g. – Omalizumab)
4. Leukotriene modifiers (E.g. Monteleukast)
5. Long Acting β_2 – Agonists (LABAs). E.g. – Salmeterol and Formoterol

1.2.5.1.2 Quick – relief medications

1. Antimuscarinics
2. Short Acting β_2 – Agonists (SABAs). E.g. – Albuterol, Levalbuterol, and Pirbuterol, Salbutamol
3. Systemic corticosteroids

Some of the Medications are explained below:

Inhaled corticosteroids (ICS) have fundamentally changed the development and course of asthma over the last decades. This is the only drug class that is proven to decrease asthma mortality. An improvement in lung function with an emphasis on the benefit of early inhaled steroid introduction has been established as well as improvement in quality of life, exacerbations and hospitalisations.Different aspects of asthma have shown different time courses for improvement, with bronchial hyperresponsiveness being particularly slow and may still continue to improve 1 year after introduction of ICS medication. The relationship between the anti-inflammatory and remodeling modulating effects of corticosteroids in asthma in relationship with clinical and functional aspects is of considerable interest. With its wide anti-inflammatory potential, it could be expected that ICS would be able to 'cure' asthma. In clinical practice, most patients experience a fundamental improvement of asthmatic symptoms, and the prognosis of asthma also improves. Still, it appears that basic underlying mechanisms in asthma persist, and may make asthmatic symptoms reappear earlier or later in life and those corticosteroids cannot be seen as the ultimate 'curing' agent. The asthmatic airway remodeling processes may to some extent be improved by ICS. The effects are varying between investigations but include improvement of epithelial damage, reduction in inflammatory cells in particular eosinophils and T-cells. The RBM thickening may be at least partly reversible with reduced tenascin deposition, (Sandström, 2010).

The effects of **β_2 – agonists** on airway remodeling have been addressed in some animal models of asthma. It can be noted that investigations in rats have suggested potential adverse effects by salbutamol treatment. An increased bronchial

hyperresponsiveness and goblet cell hyperplasia have been common events in allergen sensitized rats. Continuous treatment with salbutamol over 4 weeks was almost doubled bronchial responsiveness to metacholine, but also doubled the numbers of goblet cells. The goblet cell hyperplasia was not present in non-salbutamol treated animals and was completely abolished by prednisolone. Cell experiments have pointed towards G-protein receptor coupled stimulation by s-albuterol on mitogenic factors stimulating smooth muscle hyperplasia. This may be counteracted by the levo-albuterol isomer. Cell culture experiments with human fibroblasts have shown salbutamol, formoterol and beclomethasone alone, and in combination, to give suppressive effects on fibroblast proliferation and fibrotic remodeling processes. Several bronchoscopy studies have been performed in asthmatics investigating local airway effects of b2-agonists. To the major extent, these studies have been focused on and demonstrated suppressive effects on inflammatory cells like eosinophils and mast cells, rather than structural changes related to remodeling processes. This appears partly to reflect the research questions of the time when they were performed. Effects of combination therapy with long acting b2-agonist (LABA) and inhaled corticosteroid treatment on remodeling aspects of asthma have recently been reported. Thirteen patients with mild to moderate asthma were investigated with bronchoscopy and biopsy sampling before and after 6-month treatment with formoterol and budesonide. Baseline data were also compared with a 10-subject control group and the asthmatic subjects showed clear evidence of airway remodeling correlating positively with bronchial hyperresponsiveness and negatively with lung function. Following 6-month treatment, vascular endothelial growth factor (VEGF) and VEGFreceptor- 1 (VEGFR1) expressions in the airways were significantly reduced and

this correlated with indications of decreased remodeling changes in the airways. The authors reported significant reductions in submucosal gland hyperplasia, smooth muscle mass, RBM thickness and subepithelial fibrosis. In a subsequent in-vitro study, treatment with Salmeterol alone and in combination with Fluticasone was shown to give a similar inhibition of VEGF together with fibroblast growth factor-2 (FGF-2) in BEAS-2B cells after incubation with rhinovirus, a common trigger in asthma. Antileukotriene Cysteinyl-leukotrienes are potent bronchoconstrictive agents with pro-inflammatory properties shown to be of importance in asthma. Potential modulating effects by Monteleukast on allergic inflammation and airway remodeling have been investigated in some rat and mouse models. Interestingly, Monteleukast treatment has been shown to reduce smooth muscle hyperplasia as well as collagen deposition in the airways in allergen-sensitized rodents. These effects correspond with remodeling changes in asthma in humans, which are associated with reduced bronchial hyperresponsiveness. Further development of this research line is consequently of interest. Leukotriene antagonist treatment has over the last years found its way into clinical practice of asthma. Bjermer and co-workers reported from a large-scale study that they found relatively similar effects of Monteleukast to those of LABA. Comparative studies with inhaled corticosteroids at different doses have mainly been performed with Monteleukast vs. Fluticasone propionate (FP). In one study, 28 asthmatic subjects underwent bronchoscopy before and after 8-week treatment with 100 mg FP, with and without the addition of Monteleukast. No additive effects of Leukotriene antagonism were seen, in bronchial biopsies or soluble components, to those produced by the inhaled steroid alone. This has been interpreted by some authors as anti-leukotrienes not having major additive effects to those broader anti-inflammatory effects

of ICS in asthmatic subjects. Longer studies in larger groups of asthmatic subjects may be needed to determine the long-term effects, especially for the effects on remodeling, (Sandström, 2010).

Anticholinergic treatment in asthma has found its way into emergency room situations where ipratropium bromide may be inhaled, usually together with a b2-agonist. The primary indication for maintenance treatment with Anticholinergic is, however, chronic obstructive pulmonary disease (COPD). The influence of Anticholinergic treatment has nevertheless been explored in an animal model of asthma based on the hypothesis that growth factor-induced smooth muscle proliferation is enhanced by acetylcholine. Allergen challenge in guinea pigs resulted in hypertrophy of smooth muscle after 12 weeks, which was restricted to the peripheral non-cartilaginous airways. Tiotropium treatment was shown to inhibit the allergen-induced increases of airway smooth muscle mass, myosin expression and contractility. The study may therefore indicate that muscarinic M3-stimulation could increase the sensitivity of the bronchial smooth muscle for growth factors and inflammatory mediators, and that blockade could be beneficial. If so, this would be interesting to explore in human subjects with asthma or COPD, but to date no such data have been published, (Sandström, 2010).

Antileukotriene is one of several interesting approaches to block suggested eosinophilic components in asthma. An immediate success has escaped after the early studies in asthmatics with IL-5 antagonism. The rationale for this approach has been the perception that eosinophils and eosinophils-derived TGF-b may play a major role in chronic asthma and airway remodeling. Reductions in blood and induced sputum eosinophils have been shown in trials in asthmatic subjects, but the reductions have not

been complete and clinical effects have been elusive. Bronchial biopsies were sampled in 24 allergic asthmatic subjects before and after 10 weeks of treatment with anti-IL-5 administration. Eosinophils numbers and eosinophils TGF-b mRNA reduced together with significant reduction in tenascin, lumican and procollagen-III expression in the RBM compared with placebo, (Sandström, 2010).

Anti-IgE treatment of Omalizumab is the first antibody treatment against asthma that has hit the market worldwide. The label refers to allergic asthma with more severe cases in focus in Europe, with wider indications in the United States and certain other areas of the world. Overall, the clinical evidence supports the fact that this medication facilitates a reduction in the dose of oral and inhaled glucocorticoids in patients with allergic asthma. Biopsy sampling both from the nose and from bronchi has demonstrated significantly reduced mucosal inflammatory cell infiltration including eosinophils, T-cells and B-cells and IL-4 positive cells (30, 31). This was accompanied by suppression of the number cells positive for the high-affinity IgE receptor (FCeRI) as well as overall IgE positive cells. Data on structural changes related to remodeling of the asthmatic airways are yet to emerge and are important for a more complete understanding of this immune modulating treatment in asthma, (Sandström, 2010).

1.2.5.2 Bronchial Thermoplasty

‘Bronchial Thermoplasty refers to an electromechanical treatment using radiofrequency ablation whereby the airway wall is heated by a wire instrument inserted through the bronchoscopy channel. This particular treatment has been suggested to give a permanent effect on the smooth muscle in the airways walls, but little effect on the surrounding tissue, (Sandström, 2010).

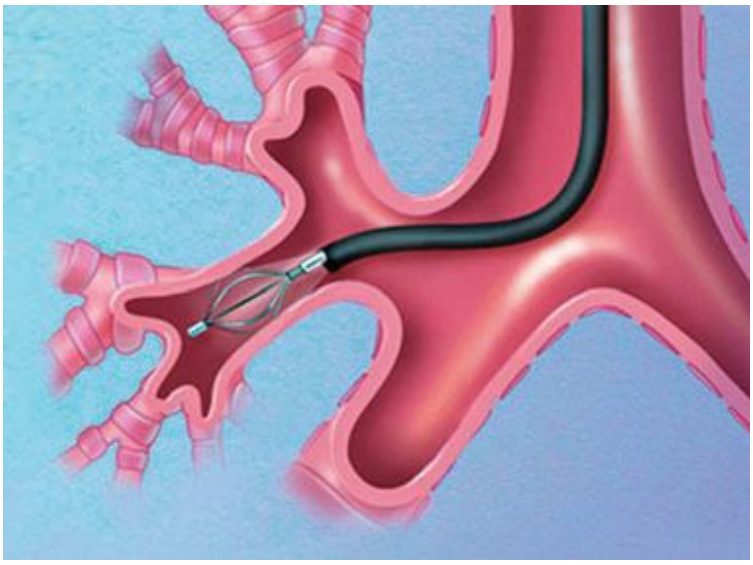


Figure 4: Bronchial Thermoplasty illustration (Sandström, 2010)

However, a drawback of such procedure is that, 'The asthmatic subjects treated with bronchial thermoplasty would have experienced an irreversible destruction of airway smooth muscle and reversible damage to other parts of the airway mucosa, in the parts of the major bronchi which were treated, (Sandström, 2010).

1.3 Prevention of Occupational Asthma

Primary prevention aims to avert the onset of disease. Secondary prevention aims to detect disease at an early or pre-symptomatic stage for example by health surveillance. Tertiary prevention aims to mitigate the effects of established disease and is considered later under the management of an identified case of occupational asthma, (Nicholson, Cullinan, Burge, & Boyle, 2010).

The most effective measure is primary prevention of exposure either by substituting the agent with a less harmful material or by engineering and hygiene measures. The following steps can be taken to prevent Occupational Asthma –

1.3.1 Prevention by Controlling Exposure

Extensive evidence of a direct relationship between occupational asthma and exposure to airborne allergens has shown the effect of reducing exposure on the incidence of occupational asthma. This reduced exposure leads to fewer cases of sensitization and occupational asthma demonstrated with acid anhydrides, detergent enzymes, laboratory animals and latex, (Nicholson, Cullinan, Burge, & Boyle, 2010).

1.3.2 Prevention by Using Respiratory Protective Equipment

Respiratory protective equipment can only offer protection when it is worn properly, removed safely and either replaced or maintained regularly. Brief periods of respirator removal might permit a transient, yet sufficiently high exposure to sensitize a worker and lead to subsequent development of asthma, (Nicholson, Cullinan, Burge, & Boyle, 2010).

1.3.3 Prevention by Pre-replacement Examinations

Pre-placement examinations should be used to establish a baseline for periodic health surveillance rather than to detect and exclude susceptible individuals from high-risk workplaces.

The efficiency of screening out susceptible job applicants depends, in part, on the frequency of the trait in the general population. Risk markers such as atopy, smoking and genetic predisposition lack sufficient sensitivity and specificity can be used to screen out job applicants, (Nicholson, Cullinan, Burge, & Boyle, 2010).

1.3.4 Prevention by Health Surveillance

Periodic health surveillance for occupational asthma aims to identify sensitized workers or cases of asthma at early and reversible stages of disease.

1.4 Guidelines to Manage Occupational Asthma

Doctors use the 'Asthma Guidelines' as a way to manage a patient's asthma. Some of the most popular asthma guidelines that most doctors follow are:

1. The National Heart Lung and Blood Institute guidelines for diagnosis & treatment of asthma British Guideline on the management of asthma
2. The National Asthma Education and Prevention Program (NAEPP) guideline
3. GINA (The Global Initiative For Asthma) Guideline
4. AAAAI (American Academy of Allergy Asthma and Immunology) Practice Guideline
5. Guidelines for the Diagnosis and Management of Asthma by American Academy of Pediatrics
6. US Asthma Management Guidelines
7. Canadian Thoracic Society guidelines for Occupational Asthma
8. British Occupational Health Research Foundation (BOHRF)

The **British Occupational Health Research Foundation** (**BOHRF**) has founded a standard guideline especially to manage Occupational Asthma for –

1. Employers and their health and safety personnel

2. Health practitioners

3. Employers, their health and safety personnel and health practitioners

1.4.1 Guidelines for Employers and their Health and Safety Personnel

According to British Occupational Health Research Foundation (BOHRF), (Nicholson, Cullinan, Burge, & Boyle, 2010)Employers and their health and safety personnel should–

1. Be aware that the major determinant of risk for the development of occupational asthma is the level of exposure to its causes and should implement programmes to remove or reduce exposure to its causes.

2. Be aware that respiratory protective equipment does not completely prevent occupational asthma and ensure that when it is worn, the appropriate type is used and maintained, fit testing is performed and workers understand how to wear, remove and replace it.

3. Inform workers about any causes of occupational asthma in the workplace and the need to report any relevant symptoms as soon as they develop.

4. Provide workers at risk of occupational asthma with health surveillance at least annually and more frequently in the first years of exposure.

1.4.2 Guidelines for Health Practitioners

According to British Occupational Health Research Foundation (BOHRF) (Nicholson, Cullinan, Burge, & Boyle, 2010), Health practitioners should –

1. Not use poorly discriminating factors - such as atopy, cigarette smoking or a family or personal history of asthma which may increase individual susceptibility to occupational asthma for some agents - as a reason to exclude individuals from employment.

2. Enquire about pre-existing occupational asthma to agents that job candidates might be exposed to in their new job and advice affected candidates that they should not undertake this work, if exposure cannot be adequately controlled.

3. Provide more frequent health surveillance to workers who develop rhinitis when working with agents known to cause occupational asthma and ensure that the workplace and working practices are investigated to identify potential causes and implement corrective actions.

4. Enquire of any adult patient with new, recurrent or deteriorating symptoms of rhinitis or asthma about their job, the materials with which they work and whether their symptoms improve regularly when away from work.

5. Confirm a diagnosis of occupational asthma by objective criteria (functional, immunological, or both) and not on the basis of a compatible history alone because of the potential implications for future employment.

6. Arrange for workers who they suspect to have occupational asthma to perform serial peak flow measurements at least four times a day and for at least three weeks.

1.4.3 Guidelines for Employers, their health and safety personnel and health practitioners

According to British Occupational Health Research Foundation (BOHRF) (Nicholson, Cullinan, Burge, & Boyle, 2010), Employers, their health and safety personnel and health practitioners should –

1. Take measures to protect workers diagnosed as having occupational asthma from further exposure to its cause in the workplace.

Chapter 2

LITERATURE REVIEW

Chapter 2: Literature Review

From the small proportion of exposed workers who develop Occupational Asthma (OA) due to persulfate salts, the latent period between onset of exposure and the onset of symptoms, and the type of response observed in the challenge test suggest that persulfate-induced OA is mediated by an immunologic mechanism. The results obtained in the present study suggest that this immunologic mechanism might be mediated by IgE, since a skin-prick test that is positive for persulfate salts had been obtained in five patients (62%), as also has been observed in approximately 50% of the cases that have been published to date. Furthermore, elevated serum total IgE levels were observed in six patients, and one patient experienced an anaphylactic reaction. Both events also have been described by other authors. However, other mechanisms also may be involved. It is suggested that mast cells may play a role in the pathogenesis of the late asthmatic reactions following the inhalation of persulfate salts, since they found a significant rise in serum neutrophil chemotactic activity paralleling airflow obstruction. Finally, T cells may play a role in the pathogenesis of OA due to persulfate salts after reporting a case in which skin-prick test positivity was observed after 24 h and histologic examination of the patient's late reaction demonstrated a perivascular infiltration predominantly comprising T lymphocytes. This late response to the skin test was not observed in any of our patients. The diagnosis of OA is usually suggested by clinical history; however, it is often not sufficient to reach a definitive diagnosis29 and should be complemented by serial measurements of PEF, immunologic testing, and/or bronchial challenge testing. Immunologic tests are of little use for the diagnosis of persulfate-induced OA since the

sensitivity and specificity of the skin-prick test, which in our series was positive in five of eight patients, remain unknown. In this respect, a 1995 study13 showed that 8 of 52 subjects who had been exposed to persulfate salts had positive skin-prick tests, regardless of whether they had experienced respiratory symptoms or not. On the other hand, in the different works published in which a specific IgE to persulfate salts was studied, no positive values could be found. In our experience, the PEF study proved useful since a response that was consistent with OA was elicited in all but one of the patients in whom it could be performed. Conversely, only one of four patients showed a consistent response, and published a case in which the PEF study was also negative. Bearing in mind that the main exposure to persulfatesalts occurs in hairdressers, who also may be exposed to other agents (such as henna30 or paraphenylenediamine31) that also can cause OA, or to different nonspecific irritants that are capable of triggering bronchospasms in individuals with or without asthma, the performance of specific challenge tests for persulfate salts may be indicated in many patients. Different methods of performing this test have been used. Some authors have carried out the test by attempting to reproduce the conditions in the workplace, others by aerosolizing a potassium persulfate nondialyzed extract by a nebulizer. Finally, the test was performed by mixing 30 g bleach powder with 50 g lactose and tipping it from one tray to another 30 cm away in a challenge chamber with independent air extraction. In the latter study, three patients also were challenged with persulfate salts; however, the authors did not detail the characteristics of the mixture. In the present study, the test was performed on consecutive days with the quantity of potassium persulfate increased and mixed with lactose with the following two objectives: to avoid overexposure in potentially sensitive patients; and to

attempt to show a possible dose response relationship, which was observed in patients 1, 2, and 4 of our series. Late response was the most frequently observed form both in our patients and in those in the literature, although three cases of early responses and one of dual response16 also have been reported, (Muñoz, Cruz, Orriols, Bravo, Espuga, & Morell, 2003).

The present study describes clinically examined patients with OA diagnosed by positive stainless steel welding challenge tests. The diagnosis of OA was based on a history of exposure, respiratory symptoms and clinical examinations including positive challenge tests. During the 10-yr period of the present study, 34 OA cases were diagnosed at the FIOH, which gives an occurrence of OA of 3.4 cases per year. It is estimated that there are 13,000 full-time welders in Finland; however, it is difficult to describe how many of these perform only or mainly welding on stainless steel. One crude estimate is 2,000–4,000, which is based on the Register of Workers at Risk of Being Exposed to Carcinogenic Substances and Processes (the register is maintained at the FIOH). All employers must report workers who are exposed significantly to carcinogens to this register; the carcinogens concerning welding are hexavalent chromium and nickel. When using this estimate for the number of stainless steel welders in Finland, this gives an incidence of OA 0.0009–0.002 per worker per yr. The mean duration of exposure to welding fumes before the onset of the respiratory symptoms was long: 18 yrs. This time refers to the duration of the occupation rather than to the actual exposure time. Although all the present patients were exposed to stainless steel welding fumes, it was impossible to estimate the true amount of this exposure because the information was based on patient interviews without measurements being taken at the working sites. A similar duration has

been reported earlier in case studies of stainless steel welding, but shorter intervals have also been described in stainless steel welding case studies or welding of other materials. The observed differences between studies could be explained by the intensity of exposure to welding fumes, welding methods and materials, common ventilation of the welding area and the use of a personal respiratory protective device. The diagnosis of OA was generally made within 4 yrs of the onset of respiratory symptoms, although in individual cases the respiratory symptoms had clearly lasted longer. In the latter cases, the diagnosis may have been delayed by a lack of awareness of this disease among healthcare professionals or because of reluctance on the part of the patients to admit work-related symptoms. In published case reports, the interval between the onset of respiratory symptoms and the diagnosis of OA has ranged from an immediate occurrence up to 8 yrs.Besides work-related respiratory symptoms, nasal or laryngeal symptoms were also common. These have been described previously among welders. Although nearly two-thirds of the present patients reported such symptoms, no diagnosis of occupational upper respiratory tract disease was made based on the otorhinolaryngological findings observed during the challenge tests. This is compatible with previous studies: to the present authors' knowledge, no cases of challenge test positive occupational rhinitis associated with welding fumes have been published, although such a case has been described dealing with occupational laryngitis. None of the patients in the present series showed positive allergic reactions to tested metal salts in SPT. This test negativity is in accordance with previous studies in which these tests have been performed. In contrast, a recent study showed that nearly 12% of welders had at least one positive SPT to a metallic salt solution (aluminum, cadmium, chromium, copper, iron, manganese, nickel

or zinc).However, skin sensitization was not significantly associated with symptoms of welding-related asthma, (Hannu, Piipari, Tuppurainen, Nordman, & Tuomi, 2007).

Exposure to asbestos will continue to be a public health challenge in many countries, despite increased efforts to ban asbestos internationally. According to updated information from the WHO, more than 107 000 people die each year from asbestos-related lung cancer, mesothelioma and asbestosis, and one in every three occupational cancer deaths is attributable to asbestos. In this study, we prospectively followed a heavily exposed group of asbestos workers, with average 25 years of exposure, for 37 years. The concentrations of either total dust or fibers far exceeded the already lenient national standards (2 mg/ m3 before 2001, and 0.8 mg/m3 and 0.8 f/ml since 2002). According to factory records, only chrysotile was ever used in the factory. Although not all samples of asbestos historically used were available, the analyses of available samples have indicated that the contamination of amphibole was very low. Since the 25-year study, the number of deaths in both cohorts had nearly doubled, which enhanced the statistical power of the study. In addition, we analyzed mortality from gastrointestinal cancer and non-malignant respiratory diseases in the cohort, which were not reported previously. We observed 53 lung cancer deaths, accounting for a fifth of all deaths in the cohort. An additional 81 (31%) workers died of non-malignant respiratory diseases, including asbestosis and related complications. Age-adjusted mortality from lung cancer and respiratory diseases in the asbestos workers was as high as 9.6 and 6.4 times that in the controls, respectively, suggesting that asbestos-related lung cancer and respiratory diseases were major causes of deaths in these workers. The results were corroborated in the multivariate analyses, showing the greatest risks associated with the exposure for lung

cancer and nonmalignant respiratory diseases. The estimated risk for either mortality outcome was over three times that in the controls. In comparison with the controls, even those at the low exposure level had a twofold risk for lung cancer death and a 2.5-fold risk for death from respiratory diseases. Moreover, the analyses showed a clear exposure response trend, with a six fold risk of lung cancer death at the high exposure level. A similar gradient was also seen in non-malignant respiratory disease deaths, with a nearly fivefold risk for those at the high exposure level. These results suggest strong associations between asbestos exposure and lung cancer and non-malignant respiratory diseases. The carcinogenicity of asbestos has been well recognized for over half a century. However, the association between exposure to chrysotile asbestos and lung cancer remains a topic of interest, as this type has been, and continues to be, widely used in many countries. In addition, the debate about the relative carcinogenicity of chrysotile and amphiboles is ongoing. Existing data from cohort studies conducted in the asbestos textile industry, though limited in number, have provided evidence for a positive association between chrysotile and lung cancer. There is an increasing consensus that there is virtually no difference between lung cancer risks presented by the different fiber types. Retrospective cohort studies in South Carolina textile workers observed SMR for lung cancer that was twofold that of the general population with an exposure response relationship. A recent retrospective cohort study in North Carolina observing workers employed for at least 1 day in any of four asbestos textile plants also reported a nearly doubled SMR for lung cancer and an increased risk with cumulative fiber exposure.7 Another retrospective cohort study conducted in Italian workers employed for at least 1 month in an asbestos textile company showed a similar finding of increased lung cancer

mortality. On the other hand, most of the previous studies were limited by their retrospective design, particularly the use of historical data and a lack of smoking information in study subjects, (Wang, et al., 2012).

The costs due to job-related COPD and asthma are estimated to be $6.6 billion in 1996. The costs are borne by diseased workers and their families, by all workers through lower wages, and by taxpayers and businesses. The magnitude of these costs justifies more attention to prevention of obstructive lung disease associated with workplace exposures in parallel with efforts to reduce smoking-related morbidity and mortality. The estimation on the cost of asthma in 1985, for persons aged 18 years, was $1.2 billion for direct costs and $1.3 billion for indirect costs. To compare these estimates to ours, we must make several adjustments. First, the prevalence of asthma has more than doubled among persons aged 18 to 44 years and among persons 65 years of age. It has increased nearly 50% among persons aged 45 to 65 years. These increases reflect a higher incidence of disease, as well as a larger population at risk. An 80% increase in prevalence, averaging across all age groups results in a corresponding 80% increase in costs from 1985 to 1996. Second, we must account for inflation. The consumer price index for medical care, which applies to direct costs, increased 105.3% from 1985 to 1996.46 The employer cost index, which applies to indirect costs, increased 42.7% from 1985 to 1996. Thirdly, the estimation for persons aged 18 years included only hospital and physician costs. These costs constitute roughly 67% of nonadministrative medical expenditures. Incorporating all three of these adjustments of the total cost of asthma in 1996 would be $9.9 billion ($6.6 billion for direct costs, $3.3 billion for indirect costs), (Leigh, Romano, Schenker, & Kreiss, 2002).

Logistic regression analysis showed that all ABC PEF scores were significant predictors of occupational asthma, with the best being ABC per hour from waking (odds ratio, 11.9 per 10 L/h/min; 95% confidence interval, 10.8 to 13.1). ROC curve analysis showed that a difference of 15 L/min/h provided a high specificity without compromising sensitivity in diagnosing occupational asthma. Analysis of data set 2 confirmed a specificity of 100% and sensitivity of 72%. Conclusion: The ABC PEF score is sensitive and specific for the diagnosis of occupational asthma and can be calculated from a shorter PEF surveillance than is needed for the current Oasys-2 work effect index. This study has developed a new scoring system for occupational asthma based on serial PEF measurements analyzed by Oasys-2 software. Using the average 2-h plot of PEF on days on and off work, by clock time, or time from waking up. We found that all scores investigated were significant predictors of occupational asthma. Furthermore, a score based on the area between rest-day and workday curves per hour from waking was the strongest predictor of occupational asthma and explained the largest proportion of variability (R^2). The analysis of different cutoff points for the score showed that using an ABC of 15 L/min/h provided a sensitivity of 68 to 72% and a specificity of 100%. A cutoff score of 10 L/min/h increased sensitivity to 78% and reduced specificity of 98% in set 2, and reduced specificity to 88 to 90% in set 1. In comparison, the currently used Oasys-2 WEI (based on a discriminant analysis of the PEF on workdays and rest days using the maximum, minimum, and mean daily plot) has a sensitivity of 76% and specificity of 94% using a cutoff of 2.51.12 Thus, the ABC per hour from waking score shows a slightly smaller sensitivity and higher specificity using the cutoff score of 15 L/min/h. Four of 11 occupational asthma-positive records that were positive using the

WEI and negative using the ABC score had an ABC score 10 L/min/h. Two of three records were positive by the ABC score and negative using the WEI and had a WEI 2.0. This may indicate that the two scoring systems are useful for different types of records. The ABC per hour from waking score was calculated from records containing at least 4 day shifts, 4 rest days, and six readings per day. Analysis of minimum data requirements for the current Oasys-2 WEI indicated that at least three complexes of data (i.e., approximately 3 weeks of recording), four PEF readings per day for 75% of the record, and 3 consecutive days in any work period are required to give a sensitivity of 78% and a specificity of 92%.17 If the data quantity is any less, the sensitivity and specificity of the WEI fall to 64% and 83%, respectively. This means that when the data quantity needed for a sensitive and specific WEI is not reached, the 2-h PEF plot can still give a reasonably sensitive and highly specific ABC score. This is an important improvement, because keeping PEF records for long time periods is usually an effort for patients, so this diagnostic score should improve patient adherence. The current analysis is confined to day shifts, so it is yet unknown how the type of shift could influence this new score, (Moore, et al., 2009).

Allergic occupational asthma is frequent in farming populations. As educational interventions can improve disease management, the short-term effect of an educational intervention in asthmatic farmers was evaluated on the basis of spirometric indices and exhaled nitric oxide fraction (FeNO). Farmers with occupational asthma (n=581), mostly sensitized against cow dander and storage mites, participated in a 1-day educational programme. Outcome measures were assessed at baseline and after 4–6 weeks, using FeNO, lung function and a questionnaire. Results were compared with those of a control

group without intervention (n=524). In the educational group, the proportion of subjects reporting work-related symptoms was reduced after the intervention. The FeNO decreased from a geometric mean of 28.2 to 25.7 ppb, and, in subjects with an elevated (.35 ppb) baseline FeNO (n=532), from 59.7 to 49.2 ppb. The corresponding changes in the control group were 25.6 versus 27.7 ppb and 49.5 versus 48.1 ppb. Spirometric results were unaltered in the two groups. Thus exhaled nitric oxide fraction, a marker of allergic airway inflammation, indicated a beneficial effect of a short-term educational intervention in farmers with occupational asthma. This suggests a potential for exhaled nitric oxide fraction in assessing the efficacy of preventive measures within a short time with higher sensitivity than spirometry, (Dressel, Gross, De la Motte, Su¨ltz, Jo¨rres, & Nowak, 2007).

It has become clear from the results of recent studies and systematic reviews that the proportion of new or recurrent asthma in adult life attributable to occupation is high, y10–15%. Surveillance schemes, such as SWORD in the UK, as well as compensation statistics and epidemiological surveys of high-risk workforces, have identified the major causes of OA and the occupations in which cases occur. Strikingly, during the decade since the inception of SWORD, the estimated incidence of OA (in different occupational groups) and the agents responsible have remained essentially unchanged, with the exceptions of the increasing incidence of asthma associated with latex allergy in healthcare workers in the mid – 1990s and a parallel decrease in asthma associated with isocyanate exposure. Although few in number and limited to a handful of workplaces, cohort studies of laboratory animal workers, bakery workers and acid anhydride workers in the 1990s all found that the risk of developing OA is determined less by individual

susceptibility (e.g. atopy, tobacco smoking, human-leukocyte antigen phenotype) and more by the level of exposure to its causes. In general, the higher the exposure, the greater the risk, and, by implication, lowering the level of exposure reduces the incidence of disease. It is also worth noting that factors associated with sensitization can differ according to a topic status. As a consequence, epidemiological research needs first to couple studies in which associated personal and environmental factors are well identified, then to properly assess the effectiveness of interventions designed to reduce exposure and disease incidence. Factors associated with the disease need to be identified in specific workforces in which known occupational sensitizers are present. Use of such information has recently shown that a factor significantly associated with the development of OA to laboratory animals was not atopy per se, as for almost all high-molecular-weight allergens, but, more specifically, baseline sensitization to domestic pets. Intervention studies undertaken in workforces usually and necessarily differ from the traditional randomized controlled trials of therapeutic interventions in patients, because random allocation of individuals to an intervention in the workplace is not feasible (and almost certainly unethical) and because the intervention is not blind. Several nonexperimental designs of high internal validity can be applied. A simple non- or quasiexperimental design is the "before and after" study, such as a comparison of the prevalence of symptoms before and after the introduction of a new process to reduce airborne allergen concentration. A quasi-experimental design is one in which the investigator lacks full control over the allocation and/or timing of intervention but nonetheless conducts the study as if it were an experiment, allocating subjects to groups. Inability to allocate subjects randomly is a common situation that may best be described as a quasi-

experiment. The strength of the evidence provided by such a study can be increased by making a series of prevalence measurements at intervals before and after the introduction of the new process. Extended and consistent measurements made in several workplaces where the intervention is introduced at different times in some but not all subjects (the so-called multiple-time-series design) further strengthens the evidence. Demonstrating the effectiveness of the intervention in each workplace at different times strengthens the casual inference by replication (internal validity) and it also makes it more likely that the success of the intervention will be reproduced in other situations, (Gautrin, Taylor, Nordman, & Malo, 2003).

The main result of this study was that the use of respiratory devices in farmers with occupational asthma significantly reduced the degree of bronchial obstruction, but did not provide complete protection. This was shown in 26 farmers by work-related inhalation challenge tests with natural materials. In the tests without RDs all patients experienced symptoms and their Raw, sRaw and TGV rose in a statistically highly significant way. A highly significant increase in these three parameters, compared with the baseline values, was also observed in tests using an RD, but these increases were, on average 57% (Raw), 60% (TGV) and 77% (sRaw) less than those observed when RDs were not worn. Fifteen of the 26 farmers complained of problems even when they had worn an RD and six of these required bronchodilatory treatment. These patients were male and female farmers working on small farms where the farmer and their spouse accomplished all of the work together. It was hardly possible for them to delegate the dusty work to someone else. From the allergological point of view changing their profession would be necessary, but for economic reasons almost none of the affected

asthmatics could do so. In order to reduce morbidity, organizational and hygiene measures at the workplace should be considered at an early stage, because some of the affected persons suffering from occupational asthma will face a worsening of their complaints if their exposure continues. Another reason for taking early measures is the fact that asthma improves in only half of the patients after exposure has been reduced. In Germany, agricultural compensation boards provide powered RDs (using a P2 Filter) to the affected persons as a measure of secondary prevention. These RDs eliminate 90% of all particles >0.5 μm. Measurements showed that the dust concentration used in the provocations represented the occupational conditions in a realistic way. Measurement of total dust concentrations of 100±54.3 mg·m-3 and respi-rable dust concentrations of 34.8±19.2 mg·m-3 during a work-related hay challenge. During hay work in barns they measured total dust concentrations of 36.1±24.5 mg·m-3 and respirable dust concentrations of 14.6±12.7 mg·m-3. In the present study respirable dust concentrations of 6.38 and 7.05 mg·m-3 were measured. It was reported that, in grain elevators, total airborne dust concentrations ranged from <10–780 mg·m-3. Measurement of total dust concentrations of up to 60.2 mg·m-3 during farm work. It was showed that work-related respiratory symptoms were more closely associated with the concentration of endotoxin in the bioaerosol of the work setting than with the total dust concentration. In the farm environment endotoxin levels vary from 0.01– 100 $\mu g \cdot m^{-3}$. Using natural materials did not allow differentiation between specific and nonspecific airway obstruction, but provided the opportunity to investigate the efficacy of RDs. The present study shows that the use of an RD with a P2 filter fails to prevent the development of symptomatic bronchial obstruction in most sensitized farmers exposed to work-related dust. Having

performed investigations among persons with laboratory animal allergy, though doubted that using an Airstream helmet could prevent the worsening of asthma. In persons exposed to grain dust, the utilization of RDs did not cause a decrease in symptoms or changes in lung function. It has been demonstrated among patients suffering from farmer's lung that the use of an RD cannot avoid the allergic reaction completely when the farmers are exposed to appropriate allergens and acute febrile reactions may even occur. It has also been shown that, among persons suffering from flour-dust asthma, RDs could not protect all patients who were exposed. This failure to protect all exposed subjects has to be attributed to filter- and face-seal leaks. The present investigation allows the conclusion to be drawn that the use of respiratory devices with P2 filters in farmers suffering from occupational asthma can reduce the development of bronchial obstruction during an acute exposition but cannot prevent it, (Wening & Neuhauss, 1998).

Chapter 3

METHODOLOGY

CHAPTER3: METHODOLOGY

3.1 Place of study

The study was conducted in **National Chest Institute**, **Dhaka Medical College**, **Gonoshasthyo Nagar Hospital** and **Central Hospital**.

National Chest Institute is one of the largest hospitals in Bangladesh dedicated and specialized for the treatment of respiratory disease. This is a government run hospital that provides treatment in very low cost. As Asthma can affect other system of the body, the hospital adopted a multidisciplinary approach to its services. Gradually, the institution has established specialized disciplines like, Cardiology, Nephrology, Surgery, etc. The Institution also conducts researches to serve the cause of providing better treatment to patients. This was the primary site for conducting the research, since most of the respondents were poor and needy.

Dhaka Medical College is the largest generalized hospital in Bangladesh. It consists of a medical college which provides medical education to its students. It is largest and most prized medical college in Bangladesh. It is also a hospital consisting of multi – disciplinary approaches towards Pulmonology, Cardiology, Gynecology, Nephrology, Gastro-enterology, Burn Unit etc. Since, it is a generalized hospital, it was also chosen as a site for conducting the research.

Gonoshasthyo Nagar Hospital is a privatized hospital situated in Mirpur Road. Though it is a privatized hospital, since it provides treatment in quiet low cost, it was

chosen as a site for conducting the research. The Hospital consists of multi – disciplinary units to cure various diseases. The Institution also has a medical college situated in Savar.

Central Hospital is a private hospital situated in Dhanmondi which was chosen as a site of conducting the research.

3.2 Method of Study

3.2.1 Study Population

In this study, 100 occupational asthma patients from National Chest Institute, Dhaka Medical College Hospital, Central Hospital and Gonoshasthyo Nagar Hospital were randomly selected and interviewed. The Respondents were in between the age of 20 to 76 years among them 22 patients were females and 78 were males.

Studies on them led to a descriptive statistical data, which consist of Qualitative Data Variables such as Respondents Occupation, Gender of Respondents, Symptoms of Asthma, Parental Asthma of the respondents and Locations and time of Occupations of Respondents etc. and Quantitative Data such respondents' age

3.2.2 Research Equipments

The Equipments that were used in this study were –

1. Interview schedule and Question forms
2. Pen
3. Pencil
4. Camera

3.2.3 Method of Data collection

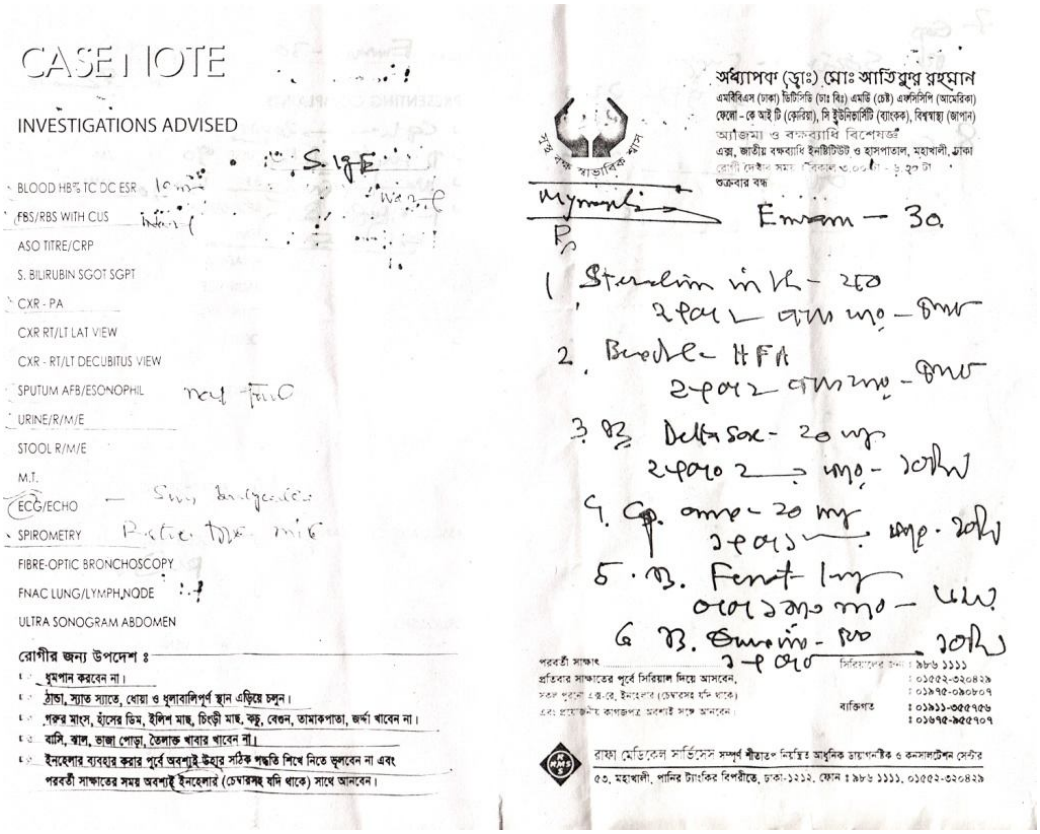
After explaining the purpose of the study to the respondents and obtaining their verbal consent, the respondents were interviewed by asking question in the Bengali and using a thoroughly pretested questionnaire.

The questionnaires was be consists of three parts.

1. Part – 1: Patients' personal information
2. Part –2: Occupation of Patients
3. Part – 3: Occupation Related Information
4. Part – 4: Treatments / Medication prescribed to the Respondents

3.2.4 Study Period

The period of conducting the research was a six month old investigation. To complete the study in time a work schedule was prepared depending on different task of the study. The two months were used for literature review, selection of topic, development of the protocol. Subsequent months were used to study on the selection of study area, data collection and tabulation, result and discussion and submission of report.



CASE NOTE

INVESTIGATIONS ADVISED

- BLOOD HB% TC DC ESR
- FBS/RBS WITH CUS
- ASO TITRE/CRP
- S. BILIRUBIN SGOT SGPT
- CXR - PA
- CXR RT/LT LAT VIEW
- CXR - RT/LT DECUBITUS VIEW
- SPUTUM AFB/ESONOPHIL
- URINE/R/M/E
- STOOL R/M/E
- M.T.
- ECG/ECHO
- SPIROMETRY
- FIBRE-OPTIC BRONCHOSCOPY
- FNAC LUNG/LYMPH NODE
- ULTRA SONOGRAM ABDOMEN

রোগীর জন্য উপদেশ ঃ

- ধূমপান করবেন না।
- ঠান্ডা, স্যাত স্যাতে, ধোয়া ও ধুলাবালিপূর্ণ স্থান এড়িয়ে চলুন।
- গরুর মাংস, হাঁসের ডিম, ইলিশ মাছ, চিংড়ী মাছ, কচু, বেগুন, তামাকপাতা, জর্দা খাবেন না।
- বাসি, ঝাল, ভাজা পোড়া, তৈলাক্ত খাবার খাবেন না।
- ইনহেলার ব্যবহার করার পূর্বে অবশ্যই উহার সঠিক পদ্ধতি শিখে নিতে ভুলবেন না এবং পরবর্তী সাক্ষাতের সময় অবশ্যই ইনহেলার (চেম্বারসহ যদি থাকে) সাথে আনবেন।

অধ্যাপক (ডাঃ) মোঃ আতিয়ুর রহমান
এমবিবিএস (ঢাকা) ডিটিসিডি (চাং বিং) এমডি (চেষ্ট) এফসিসিপি (আমেরিকা)
ফেলো - কে আই টি (কোরিয়া), সি ইউনিভার্সিটি (ব্যাংকক), বিশ্বস্বাস্থ্য (জাপান)
অ্যাজমা ও বক্ষব্যাধি বিশেষজ্ঞ
এক্স, জাতীয় বক্ষব্যাধি ইনষ্টিটিউট ও হাসপাতাল, মহাখালী, ঢাকা
রোগী দেখার সময়: বিকেল ৩.০০টা - ৬.৩০ টা
শুক্রবার বন্ধ

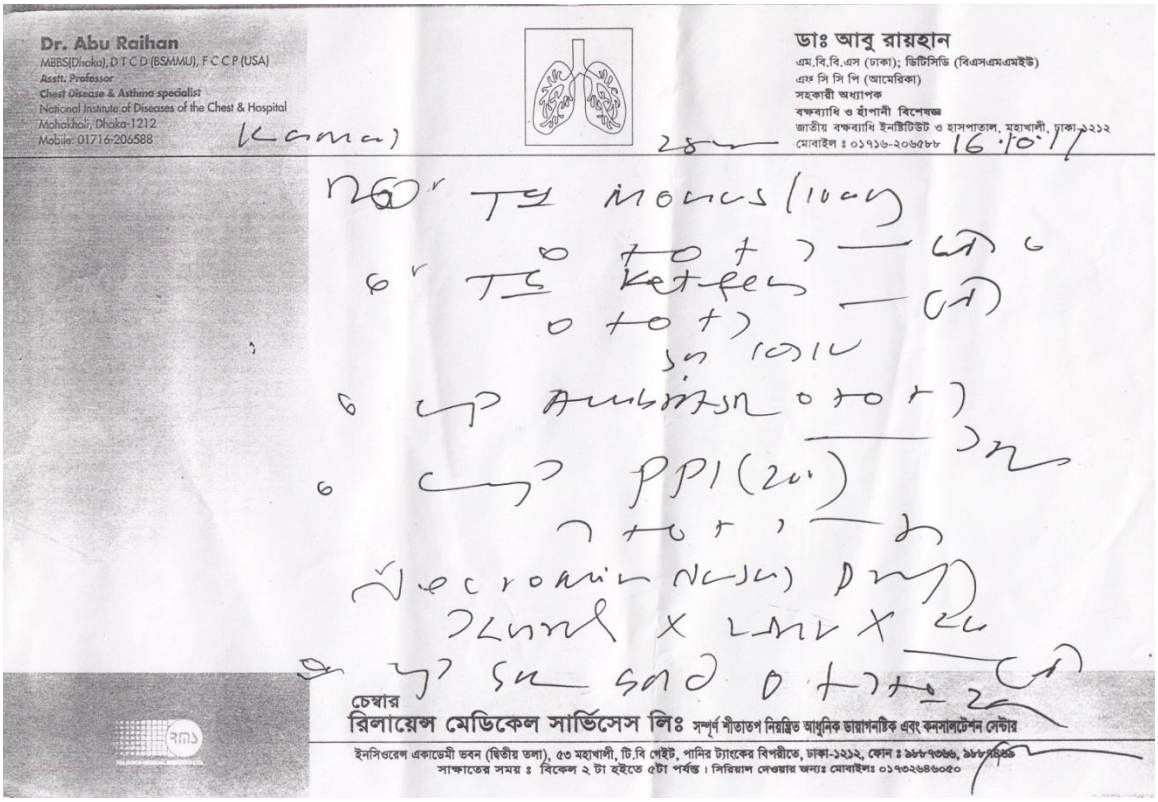
Emran – 30

1. Stemlin inh – 250
2. Breezhaler HFA
3. Deltasac – 20 mg
4. Cap. omep – 20 mg
5. B. Fenet Inj
6. B. Ceftriaxone - 500

পরবর্তী সাক্ষাৎ
প্রতিবার সাক্ষাতের পূর্বে সিরিয়াল নিয়ে আসবেন,
সকল পুরনো এক্স-রে, ইনভেস্টগেশন (চেম্বারসহ যদি থাকে) এবং প্রেসক্রিপশন কাগজপত্র অবশ্যই সাথে আনবেন।

সিরিয়ালের জন্য: ৯৮৮৬ ১১১১
০১৩৫২-৩২০৪২৯
০১৯৭৫-০৯০৮০৭
ব্যক্তিগত ঃ ০১৯১১-০৫৫৭৫৬
ঃ ০১৬৭৫-৯৫৫৭০৭

রাফা মেডিকেল সার্ভিসেস সম্পূর্ণ শীতাতপ নিয়ন্ত্রিত আধুনিক ডায়াগনষ্টিক ও কনসালটেশন সেন্টার
৫৩, মহাখালী, পানির ট্যাংকির বিপরীতে, ঢাকা-১২১২, ফোন ঃ ৯৮৬ ১১১১, ০১৩৫২-৩২০৪২৯



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Mobile: 01716-206588

ডাঃ আবু রায়হান
এম.বি.বি.এস (ঢাকা); ডিটিসিডি (বিএসএমএমইউ)
এফ সি সি পি (আমেরিকা)
সহকারী অধ্যাপক
বক্ষব্যাধি ও হাঁপানী বিশেষজ্ঞ
জাতীয় বক্ষব্যাধি ইনষ্টিটিউট ও হাসপাতাল, মহাখালী, ঢাকা-১২১২
মোবাইল ঃ ০১৭১৬-২০৬৫৮৮

চেম্বার
রিলায়েন্স মেডিকেল সার্ভিসেস লিঃ সম্পূর্ণ শীতাতপ নিয়ন্ত্রিত আধুনিক ডায়াগনষ্টিক এবং কনসালটেশন সেন্টার
ইনসিওরেন্স একাডেমী ভবন (দ্বিতীয় তলা), ৫৩ মহাখালী, টি.বি গেইট, পানির ট্যাংকের বিপরীতে, ঢাকা-১২১২, ফোন ঃ ৯৮৮৭৩৬৬, ৯৮৮৭৫৫৫
সাক্ষাতের সময় ঃ বিকেল ২ টা হইতে ৫টা পর্যন্ত। সিরিয়াল সেওয়ার জন্যঃ মোবাইলঃ ০১৭০২৬৪৬০৫০

Sample Questionnaire: Study of Occupational Asthma among Different Occupants in Dhaka

---

Personal Information

Name:_____ **Gender:** ❑ Male ❑ Female

Occupation: _____ **Working Hours per Day:**_____

Location of Working:_____ **Working Years**:_____

Information on Asthma

Parental Asthma Status: ❑ Yes ❑ No

Primary Symptoms:
- ❑ Coughing
- ❑ Wheezing
- ❑ Chest tightness
- ❑ Chest pain
- ❑ Shortness of Breath
- ❑ Sneezing

Type of Drug Administered
- ❑ Antibiotic
- ❑ Antihistamines
- ❑ Antileukotriene Inhibitor
- ❑ Combined Preparations
- ❑ Corticosteroids
- ❑ Long Acting β_2 – Agonists
- ❑ Short acting β_2 – Agonists
- ❑ Methyl xanthine Derivative

Prescribed Drugs:_____

Dosage Forms:
- ❑ Tablet
- ❑ Syrup
- ❑ Inhaler

Chapter 4

RESULT AND DISCUSSION

CHAPTER 4: RESULT AND DISCUSSION

4.1 Result

4.1.1 Age of Occupational Asthma Patients

Table 6: Age of Occupational Asthma Patients

Age	Number of Patients	Patients in Percentage (%)
20 – 28	13	13%
28 – 36	35	35%
36 – 44	26	26%
44 – 52	11	11%
52 – 60	7	7%
60 – 68	5	5%
68 – 76	3	3%
Total	**100**	**100%**

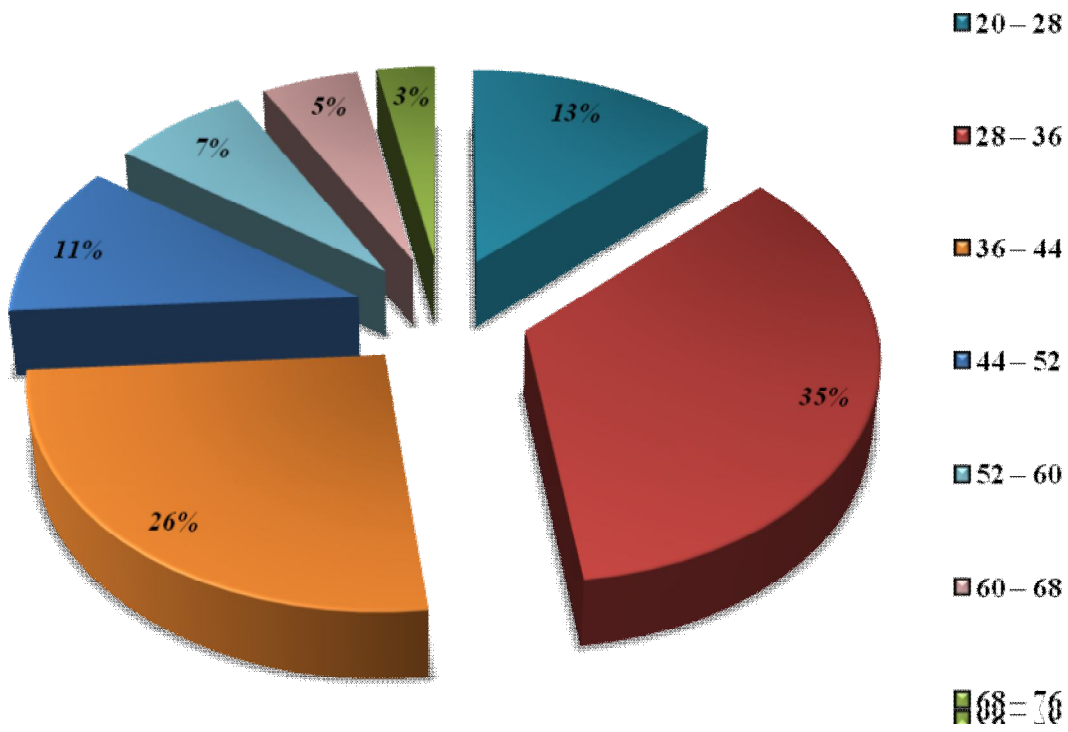

Figure 5: Graphical Representation of Age of Occupational Asthma Patients

4.1.2 Occupations of Asthma Patients

Table 7: Occupations of Asthma Patients

Occupation of Asthma Patients	Number of Patients
Beggar	3
Day Laborer	31
Rickshaw-puller	19
Fisherman	9
Garment's Worker	22
CNG Driver	16
Total	**100**

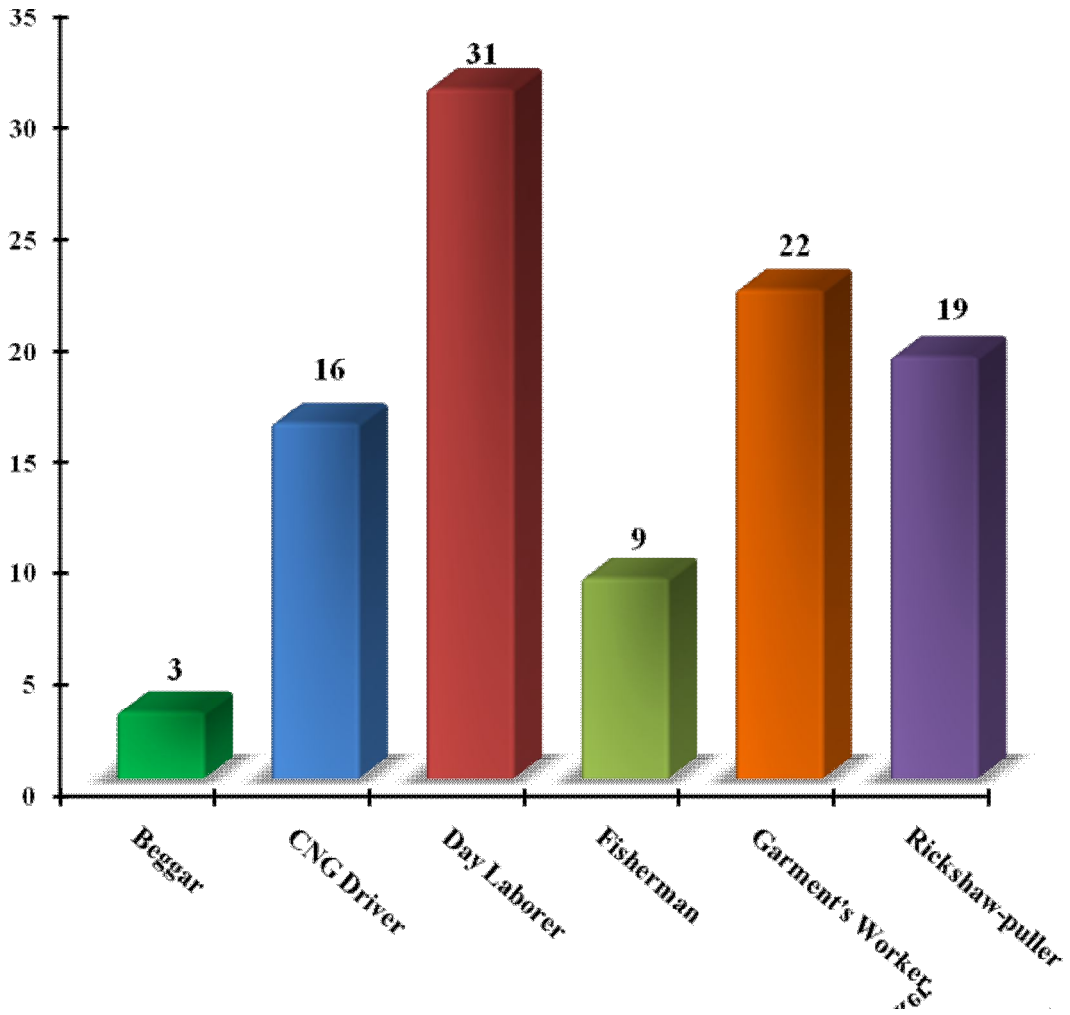

Figure 6: Occupations of Asthma Patients

4.1.3Working Period of Occupational Asthma Patients

Table 8: Working Period of Occupational Asthma Patients

Occupation	Working Period		
	6 AM to 6 PM	6 PM to 12 AM	12 AM to 6 AM
Beggar	3	0	0
Day Laborer	19	9	3
Rickshaw-puller	14	3	2
Fisherman	4	3	2
Garment's Worker	22	0	0
CNG Driver	7	7	2

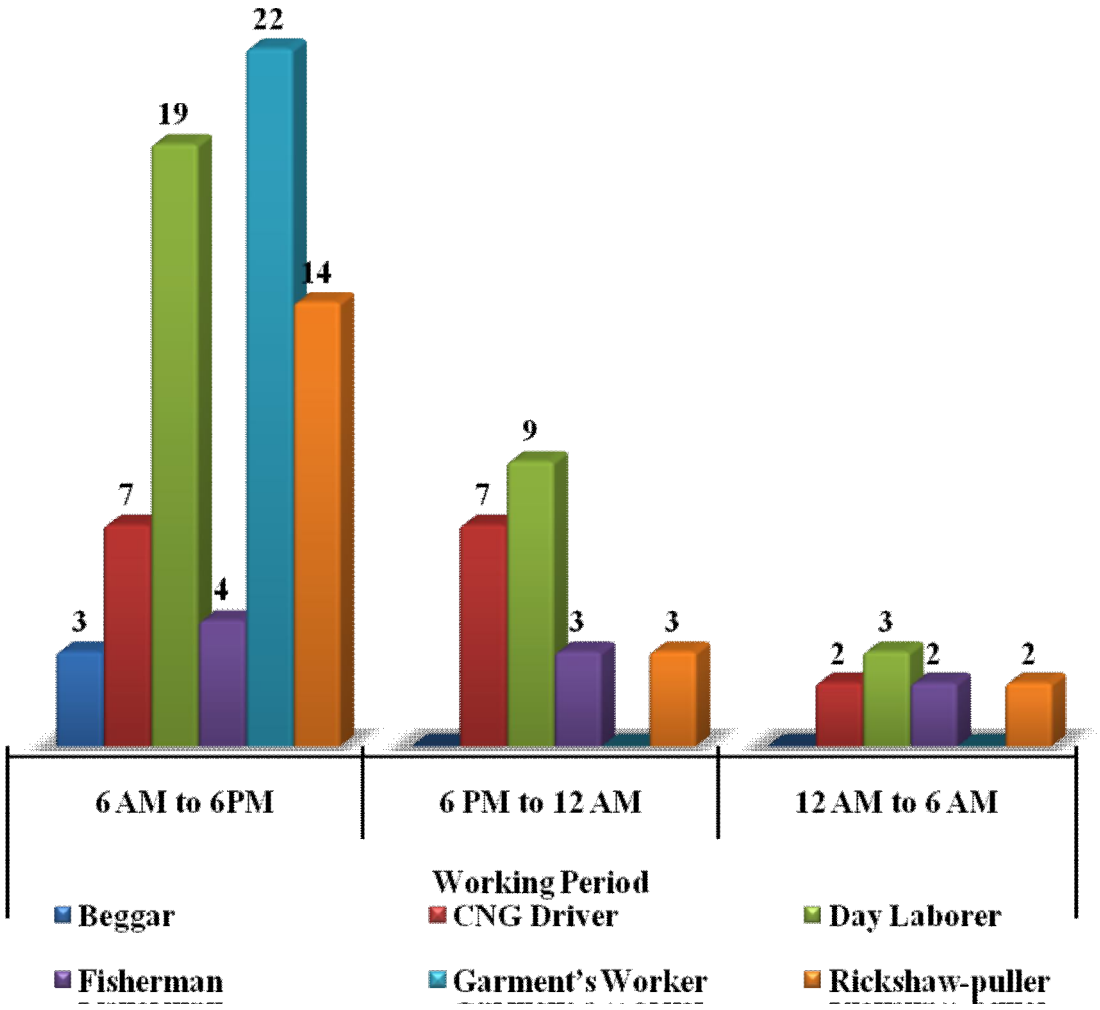

Figure 7: Working Period of Occupational Asthma Patients

4.1.4 Gender Distribution among Occupational Asthma Patients

Table 9: Gender Distribution of Occupational Asthma Patients

Occupation of Asthma Patients	Gender of Patients	
	Male	Female
Beggar	2	1
Day Laborer	28	3
Rickshaw-puller	19	0
Fisherman	9	0
Garment's Worker	4	18
CNG Driver	16	0

Total	78	22

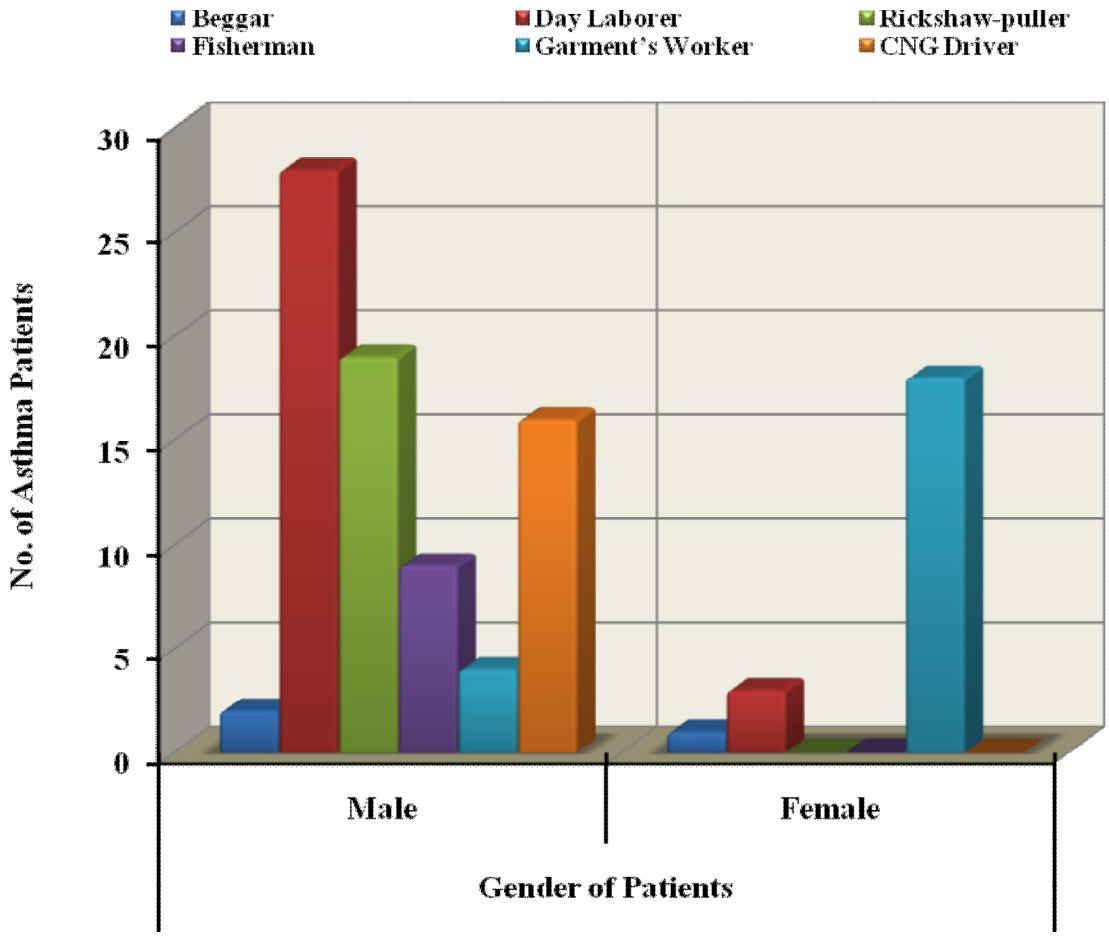

Figure 8: Gender Distribution among Occupational Asthma Patients

4.1.4 Parental Asthma Status of Occupational Asthma Patients

Table 10: Parental Asthma Status of Occupational Asthma Patients

Parental Asthma Status	Number of Patients
Yes	17
No	83

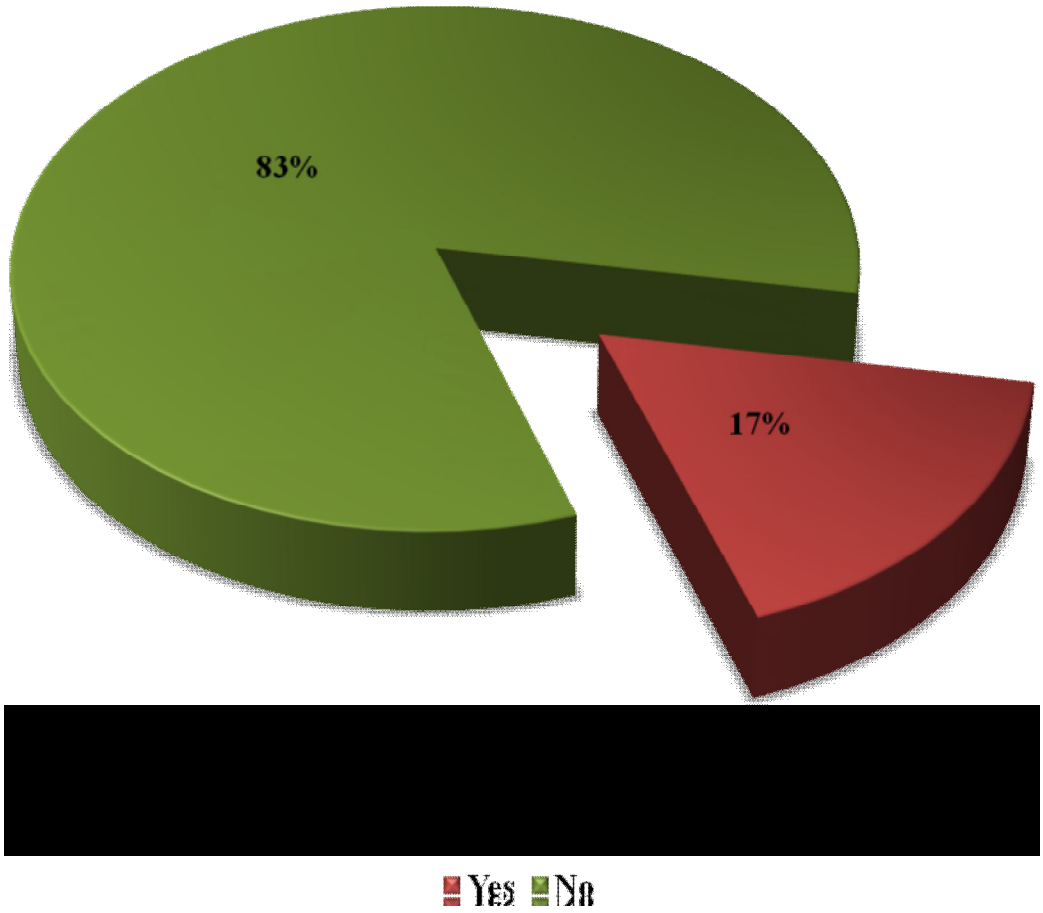

Figure 9: Parental Asthma Status of Occupational Asthma Patients

4.1.5 Locations of Occupation of Occupational Asthma Patients

Table 11: Locations of Occupation of Occupational Asthma Patients, (Locations in Dhaka, A = Mohakhali, B = Motijheel, C = Mirpur, D = Dhanmondi, E = Shadarghat; Locations out of Dhaka, F = Naryanganj, G = Tongee and H = Others)

Occupation	Locations in Dhaka					Locations Out of Dhaka			Total
	A	B	C	D	E	F	G	H	

Occupation	Locations in Dhaka					Locations Out of Dhaka			Total
	A	B	C	D	E	F	G	H	
Beggar	1	0	1	0	0	0	1	0	3
CNG Driver	4	3	5	3	0	0	1	0	16
Day Laborer	4	5	13	4	0	2	1	2	31
Fisherman	0	0	0	0	7	0	0	2	9
Garment's Worker	4	4	9	0	0	1	3	1	22
Rickshaw – puller	1	3	4	2	3	0	6	0	19
Total	14	15	32	9	0	3	12	5	100

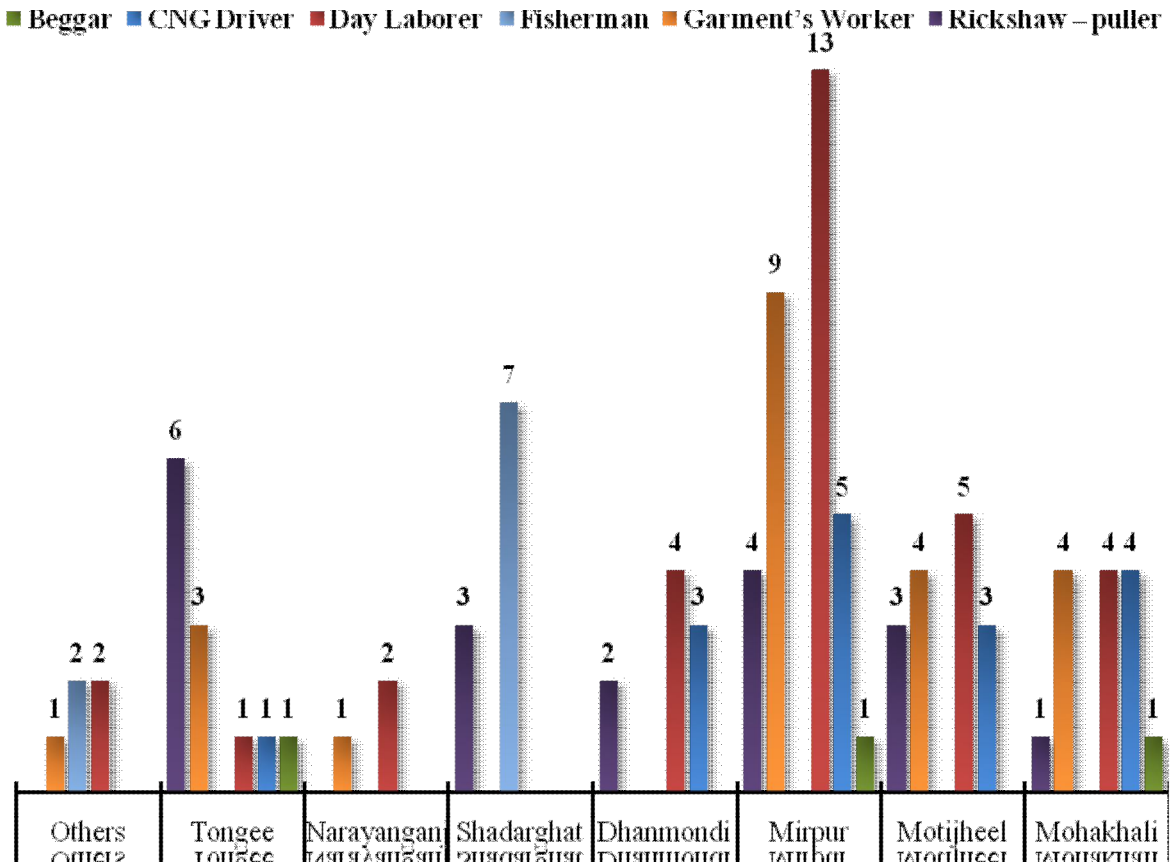

Figure 10: Graphical Representation of Locations of Occupation of Occupational Asthma Patients

4.1.6 Primary Symptoms observed in Occupational Asthma Patients

Table 12: Primary Symptoms observed in Occupational Asthma Patients

Symptoms of Asthma Patients	Number of Patients showing the symptoms
Coughing	52

Wheezing	100
Chest tightness	53
Chest pain	25
Shortness of Breath	100
Sneezing	42

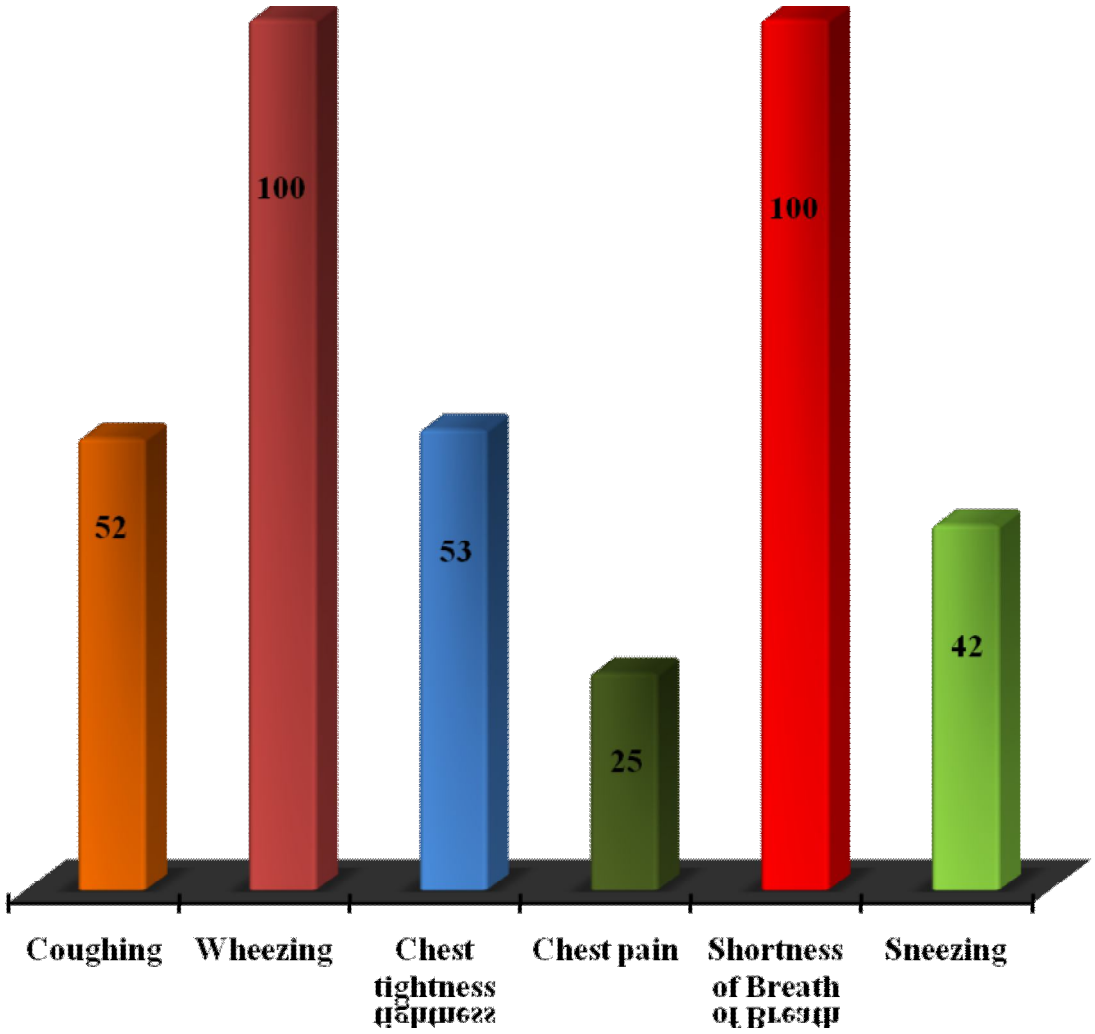

Figure 11: Primary Symptoms shown by Occupational Asthma Patients

4.1.7 Prescribed Drug to Occupational Asthma

Table 13: Drugs prescribed to Occupational Asthma

Drug Type	Brand Name	Generic Name	Company Name	Dosage Forms
Anti – Leukotriene	Monas	Monteleukast	Acme	Tablet
Anti – Leukotriene	Mokast	Monteleukast	Alco Pharma	Tablet
Antibiotic	Azyth	Azithromycin	Sandoz / Novartis	Tablet
Antibiotic	Maprocin	Ciprofloxacin	Orion	Tablet
Antibiotic	Quinox	Ciprofloxacin	SK + F	Tablet
Antibiotic	Levox	Levofloxacin	Opsonin	Tablet
Antibiotic	Sparflox	Sparfloxacin	Alco Pharma	Tablet
Corticosteroid	Oradexon	Dexamethasone	Nuvista	Tablet
Corticosteroid	Decason	Dexamethasone	Opsonin	Tablet
Corticosteroid	Precodil	Prednisolone	Opsonin	Tablet
Cough Suppressant	Dexpoten	Dextromethorphan + Pseudoephedrine + Triprolidine	SK + F	Syrup
Cromoglycate	Ketifen	Ketotifen	Acme	Tablet
Cromoglycate	Tofen	Ketotifen	Beximco	Tablet
Cromoglycate	Fenat	Ketotifen	Drug International	Tablet

Table 14: List of Drugs prescribed in Occupational Asthma

Drug Type	Brand Name	Generic Name	Company Name	Dosage Forms
Non – sedating Antihistamine	Fenadin	Fexofenadine	Reneta	Tablet
Short Acting β_2 –Agonists (SABAs)	Pulmolin – L	Levosalbutamol	Opsonin	Tablet
Short Acting β_2 –Agonists (SABAs)	Asmolex – L	Levosulbutamol	Aristopharma	Tablet
Short Acting β_2 –Agonists (SABAs)	Pulmolin	Salbutamol	Opsonin	Tablet
Short Acting β_2 –Agonists (SABAs)	Sultolin	Salbutamol	Square	Tablet
Short Acting β_2 –Agonists (SABAs)	Pulmolin	Salbutamol	Opsonin	Tablet
Short Acting β_2 –Agonists (SABAs)	Asmolex	Salbutamol	Aristopharma	Inhaler
Short Acting β_2 –Agonists (SABAs)	Ventolin	Salbutamol	Glaxo Smith Kline	Inhaler
Methyl xanthine Derivatives	Unikon	Theophylline	Ibn Sina	Syrup
Methyl xanthine Derivative	Fillin	Aminophylline	Opsonin	Tablet
LABA + Inhaled Corticosteroid	Axinat – F	Salmeterol + Fluticasone	Acme	Inhaler
Long Acting β_2 –Agonists (LABAs)	Axinat	Salmeterol	Acme	Syrup
Long Acting β_2 –Agonists (LABAs)	Bexitrol	Salmeterol	Beximco	Inhaler

4.1.8 Dosage forms of Drugs prescribed to Occupational Asthma Patients

Table 15: Dosage forms of Different Drugs prescribed to Occupational Asthma Patients

Drug Type	Prescribed Dosage Form to Patients		
	Tablet	Syrup	Inhaler
Antibiotic	37	0	0
Antihistamines	24	5	0
Antileukotriene Inhibitor	15	0	0
Combined Preparations	0	5	17
Corticosteroids	40	0	17
Long Acting β_2 – Agonists	25	15	31
Methyl xanthine Derivative	15	0	0
Short acting β_2 – Agonists	12	0	83

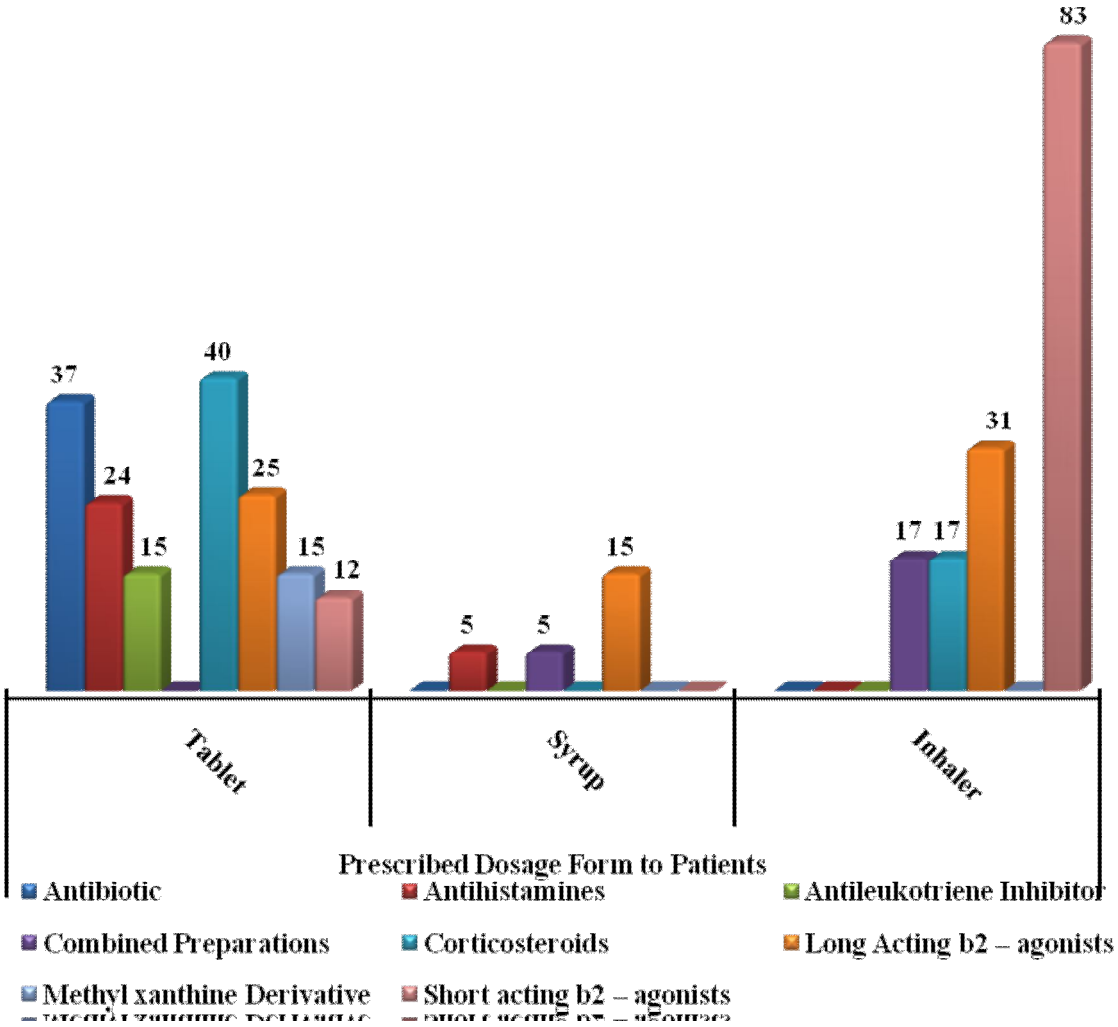

Figure 12: Dosage forms of Different Drugs prescribed to Occupational Asthma Patients

4.2 Discussion

The study was conducted on 100 occupational asthma patients from National Chest Institute, Dhaka Medical College Hospital, Central Hospital and Gonoshasthyo Nagar Hospital, who were randomly selected and interviewed. The patients were in between the age of 20 to 76 years who were distributed into 7 groups. Among these, 22 patients were females and 78 were males. In this study, six major job categories were found in asthma patients and job tasks held by the asthma patients were stable. The occupation of asthma patients were Beggars, Day Laborers, Rickshaw – pullers, Fishermen, Garment's Workers and CNG Drivers. Some of these patients worked from 6 AM to 6 PM, 6 PM to 12 AM, while some from 12 AM to 6 AM. Some of these Patients' Parents also suffered from Asthma. The patients' occupational locations were both in and out of Dhaka.

Primary symptoms of asthma observed in these patients were Coughing, Wheezing, Chest tightness, Chest pain, Shortness of Breath and Sneezing. These patients received Antibiotic, Antihistamines, Antileukotriene Inhibitor, , Inhaled Corticosteroids, Long Acting β_2 – Agonists, Short acting β_2 – Agonists, Methyl xanthine Derivative and Combined Preparations of Cough Suppressants and Corticosteroids + Long – acting β_2 – Agonist for their treatment. There are different companies of Bangladesh making these drugs available in different Brand Names. Patients received these drugs in different dosage forms available in the market.

So, the development of occupational asthma is often long. After the diagnosis of occupational asthma, the continuation of welding work becomes impossible in most

cases. The possibility of occupational asthma should be recognized not only by occupational physicians working among workers but also by pulmonologists examining patients with work-related respiratory symptoms.

The introduction of chemicals into the workplace is the main cause of it. It should be highlighted that the presence of the suspected agent in any listing of etiological causes of occupational asthma should not exclude the diagnosis. Understanding the pathogenesis of Occupational Asthma is important for the prevention and management of the condition. In this case, identifying the structural and biological characteristics that determine the potential for inducing airway sensitization is fundamental to the implementation of primary preventive strategies. Investigation of occupational asthma should be based on a stepwise approach in which multiplication and judicious use of objective means contributing to improving the quality of the diagnosis, detection and treatment.

In Bangladesh, the researches on occupational asthma have not been conducted ever before. So, there is a wide scope to emphasize on this matter. However, it is also true that the worker who are exposing to such environment which causing this type of asthma is rarely controlled. So, To start with, a national effort should be made to prepare a data base which would be most helpful to clinicians and investigators in this field and most importantly to workers exposing to such environments.

Chapter 4

CONCLUSION

CHAPTER 4: CONCLUSION

Asthma is associated with remodeling changes in the airways including increased thickening of the basement membrane region as well as other structural changes. The role of these changes has attracted considerable interest. Certain, positive effects on airway remodeling have been demonstrated following cessation of harmful occupational exposures and also to some degree for some of today's pharmacological agents. The most profound changes in airway structure have been seen following bronchial thermoplasty which reduces bronchial smooth muscle mass, associated with positive effects on asthma control at least during the limited follow-up period.

So, understanding the pathogenesis of Occupational Asthma is a crucial step toward optimal prevention and management of the condition. In this respect, identifying the structural and biological characteristics that determine the potential for inducing airway sensitization is fundamental to the implementation of primary preventive strategies. A body of epidemiological evidence has accumulated to support a dose/response relationship between the level of exposure to HMW agents and the development of OA, although application of this information to the determination of exposure limits in the workplace will require the standardization of assessment methods. Further research is needed to clarify the impact of nonrespiratory routes of exposure and concomitant exposure to pollutants in the workplace.

The pathogenesis of occupational asthma caused by low molecular weight agents remains largely uncertain, since the innate chemical reactivity of these agents has

obscured the investigation of immunological mechanisms. Available data suggest that T-cell subset and cytokine profile involved in occupational asthma caused by low molecular weight agents may differ from those operating in atopic asthma. At present, however, there is little direct evidence that immunoglobulin E-independent immunological or nonimmunological mechanisms alone are able to account for the initiation and perpetuation of occupational asthma. Recent advances in the characterization of the molecular interactions between low molecular weight agents should lead to a re-exploration of the nature of immunological mechanisms using more biologically relevant antigenic determinants.

Low socio – economic status is associated with asthma as well as asthmatic and bronchitic symptoms of Occupational Asthma found in this study. An increased risk of asthma and respiratory symptoms among the manual worker population accompanied by a marked attributable risk percent was also found. Since several longitudinal studies have recently shown an association between low socio-economic status and respiratory symptoms, I conclude that low socioeconomic status is significantly associated with an increased risk of prevalent or incident asthma and respiratory symptoms. Further clinical studies are needed to measure the exposures that increase the knowledge about the influence of possible confounders of Occupational Asthma.

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