

Effect of Air Pollution, Contamination and High Altitude on Bronchial Asthma

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Abstract:

Epidemiological studies have shown that the prevalence of asthma has risen dramatically worldwide and evidence suggests that environmental factors have an important role in the etiology of the disease. Most respiratory diseases are caused by airborne agents. Our lungs are uniquely vulnerable to contamination from the air we breathe. Air pollution exposure is associated with increased asthma and allergy morbidity and is a suspected contributor to the increasing prevalence of allergic conditions. Observational studies continue to strengthen the association between air pollution and allergic respiratory disease.

The effects of air pollution should be viewed in two different groups: healthy people and people with chronic heart or lung disease. Although the fundamental causes of asthma are not completely understood, the strongest risk factors for developing asthma are inhaled asthma triggers. These include: indoor allergens (for example house dust mites in bedding, carpets and stuffed furniture, pollution and pet dander), outdoor allergens (such as pollens and moulds), tobacco smoke and chemical irritants in the workplace. Other triggers can include cold air, extreme emotional arousal such as anger or fear, and physical exercise. Even certain medications can trigger asthma such as aspirin and other non-steroid anti-inflammatory drugs, and beta-blockers. Urbanization has also been associated with an increase in asthma; however the exact nature of this relationship is unclear. Medication is not the only way to control asthma.

It is also important to avoid asthma triggers - stimuli that irritate and inflame the airways. Prevalence of asthma is generally low within the Middle East, although high rates have been recorded in the Kingdom of Saudi Arabia, Kuwait, Lebanon, and Israel.

The prevalence of asthma and asthma-related symptoms is high among 16- to 18-year-old adolescents in Saudi Arabia, and the symptoms are more common in boys than in girls, associated with a high rate of rhinitis symptoms and hay fever. In addition to bronchial asthma, prevalence of allergic diseases in a sample of Taif citizens assessed by an original Arabic questionnaire (phase I) evidenced a high prevalence of allergic diseases as Urticaria, allergic rhinitis with or without other co-morbidities, and atopic dermatitis. Effect of high altitude on bronchial asthma is controversial; at high altitudes, the concentrations of the allergens are reduced due to the reduced amounts of vegetation, animal populations and human influences, high UV light exposure and low humidity could be contributing factors to the benefits of high altitude other than allergen avoidance. On the contrary, Lower altitudes have significant beneficial effects for bronchial asthma patients but lessen with increasing altitudes; the mountain climate can modify respiratory function and bronchial responsiveness of asthmatic subjects.

Hypoxia, hyperventilation of cold and dry air and physical exertion may worsen asthma or enhance bronchial hyper-responsiveness while a reduction in pollen and pollution may play an important role in reducing bronchial inflammation. Increasing attention has to be paid to the potential of urban air toxics to exacerbate asthma. Continued emphasis on the identification of strategies for reducing levels of urban air pollutants is warranted to reduce respiratory diseases and other diseases related to pollution. Efforts for reducing the asthma burden must focus on primary prevention to reduce the level of exposure of individuals and populations to common risk factors, particularly tobacco smoke, frequent lower respiratory infections during childhood, and environmental air pollution (indoor, outdoor, and occupational).

Introduction:

Epidemiological studies have shown that the prevalence of asthma has risen dramatically worldwide and evidence suggests that

environmental factors have an important role in the etiology of the disease. Although the fundamental causes of asthma are not

completely understood, the strongest risk factors for developing asthma are inhaled asthma triggers.

Several air pollutants are associated with asthma and chronic obstructive airway disease. Solid fuels represent a major danger in low, middle and high income countries, more than 3 billion people, almost all in low and middle income countries rely on solid fuels in the form of wood dung and crop residues for domestic energy. These materials are typically burnt in simple stoves with incomplete combustion, consequently women and children are exposed to high levels of indoor pollution every day resulting in an estimated 1.5 – 1.8 million premature deaths a year. The main health pollutants in dwellings are second hand tobacco smoke, indoor allergens, nitrogen oxide, formaldehyde, volatile organic compounds, indoor-generated particulate matter and carbon monoxide. These pollutants can affect the respiratory system and can cause or exacerbate asthma. Among all indoor pollutants, tobacco smoke is the major cause of indoor air pollution, morbidity and mortality in high, middle and low income countries (1).

I-Bronchial asthma

Asthma is a chronic condition involving the respiratory system in which the airway occasionally constricts, becomes inflamed, and is lined with excessive amounts of mucus, often in response to one or more triggers (2). These episodes may be triggered by such things as exposure to an environmental stimulant (or allergen) such as cold air, warm air, perfume, moist air, exercise or emotional stress. In children, the most common triggers are viral illnesses such as those that cause the common cold (3). This airway narrowing causes symptoms such as wheezing, shortness of breath, chest tightness and coughing. The airway constriction responds to bronchodilators. Between episodes, most patients feel well but can have mild symptoms and they may remain short of breath after exercise for longer periods of time than the unaffected individual. The symptoms of asthma, which can range from mild to life threatening, can usually, be controlled with a combination of drugs and environmental changes. Public attention in the developed world has recently focused on asthma because of its rapidly increasing

prevalence, affecting up to one in four urban children (4).

Epidemiology of bronchial asthma:

According to World Health Organization (WHO) estimates, 300 million people suffer from asthma and 255 000 people died of asthma in 2005. Asthma is the most common chronic disease among children. Asthma is not just a public health problem for high income countries: it occurs in all countries regardless of level of development. Over 80% of asthma deaths occur in low and lower-middle income countries. Asthma deaths will increase by almost 20% in the next 10 years if urgent action is not taken. Asthma is under-diagnosed and under-treated, creating a substantial burden to individuals and families and possibly restricting individuals' activities for a lifetime. The incidence of asthma is highest among low-income populations (asthma deaths are most common in low to middle income countries) which are more likely to live near industrial areas. Additionally, asthma has been strongly associated with the presence of cockroaches in living quarters, which is more likely in such neighborhoods (5).

Bronchial asthma in North Africa and Middle East

In western countries, the prevalence of asthma and allergic rhino conjunctivitis is high and has been rising throughout the late 20th century.

Little is known about the prevalence of allergic disorders in children in North Africa and the Middle East, and even less is known about the relative importance of socioeconomic factors in its etiology in these countries, when compared to Europe, the USA and Australia. The role of socioeconomic factors in the etiology of asthma is not simple. The "hygiene hypothesis" suggests that higher standards of hygiene and cleanliness have reduced the chance for cross-infection in childhood and increased the risk of atopic sensitization. Although "poor" and "richer" children living in urban environments may be equally less exposed to faeco-oral pathogens than in the past, poorer children may still have a higher exposure to many risk factors facilitating severe asthma and wheezing. Such risk factors may include airborne viruses, smoke, indoor dampness, cockroaches and poor access to healthcare, however the prevalence

of asthma is generally low within the Middle East, although high rates have been recorded in the Kingdom of Saudi Arabia, Kuwait, Lebanon, and Israel. The available evidence indicates that the prevalence of asthma has increased over recent decades throughout the Middle East. It is anticipated that, with increasing Westernization of lifestyle and continued urban shifts in population, the burden of asthma will increase considerably in coming years (6).

Prevalence of Bronchial Asthma in Saudi Arabia:

Bronchial Asthma emerged to be one of the prevalent diseases in Saudi Arabia and showed regional diversity. A study was done in pediatric department in King Saud University, shows that the socio-economic differences between asthmatic and non-asthmatic children were none striking. Environmental and geographical influences were considered to be the reasons of the variations in the rate of prevalence. Prevalence of Bronchial Asthma in school children were studied in different part of the country using a standardized protocol of 32 questionnaires. The studies revealed varying prevalence of asthma with highest 24% being in Gizan (n=362) followed by **Taif 23%** (n=594) and Hail 22% (n=507) an agricultural city. The prevalence rate of asthma for other places where as follows, Al-Gazim 16% (n=384), Abha 13% (n=485), Dammam 12% (n=889), Hofuf 14% (n=923), Jeddah 12% (n=531) and Riyadh 10% (n=988). The prevalence for allergic rhinitis was much higher than asthma (7). Another study done by **Mohammed et al (8)** to study the prevalence of asthma and associated symptoms in 16- to 18-year-old adolescents in Saudi Arabia, and concluded that the prevalence of asthma and asthma-related symptoms is high among 16- to 18-year-old adolescents in Saudi Arabia, and the symptoms are more common in boys than in girls, he also found that asthma and asthma-related symptoms are also associated with a high rate of rhinitis symptoms and hay fever and stated that the high prevalence of asthma in Saudi Arabia is within the reported prevalence ranges from many other parts of the world (8). In addition to bronchial asthma, prevalence of allergic diseases in a sample of Taif citizens assessed by an original Arabic questionnaire (phase I) evidenced a high

prevalence of allergic diseases as urticaria, allergic rhinitis with or without other co-morbidities, and atopic dermatitis, this is an important health issue which requires strategic application of primary health care facilities to achieve adequate **control (9)**.

I- Effect of high altitude on bronchial asthma

Effect of high altitude on bronchial asthma is controversial; asthma symptoms are aggravated by exposure to allergens, such as pollen, dust and air pollution. At high altitudes, the concentrations of the allergens are reduced due to the reduced amounts of vegetation, animal populations and human influences, high UV light exposure and low humidity could be contributing factors to the benefits of high altitude other than allergen avoidance (10). On the contrary, Lower altitudes have significant beneficial effects for bronchial asthma patients but lessen with increasing altitudes; the mountain climate can modify respiratory function and bronchial responsiveness of asthmatic subjects. Hypoxia, hyperventilation of cold and dry air and physical exertion may worsen asthma or enhance bronchial hyperresponsiveness while a reduction in pollen and pollution may play an important role in reducing bronchial inflammation. At moderate altitude (1,500-2,500 m), the main effect is the absence of allergen and pollutants, however at high altitudes the environment is not harmful to those with well-controlled asthma (11).

Air pollution

Most respiratory diseases are caused by airborne agents. These may be bacteria, viruses, chemicals in cigarette smoke, allergens, various gases, or dusts. Our lungs are uniquely vulnerable to contamination from the air we breathe. To this extent most lung disease is caused by air pollution or air contamination.

Air pollution exposure is associated with increased asthma and allergy morbidity and is a suspected contributor to the increasing prevalence of allergic conditions, whereas recent mechanistic studies have defined the prominent role of oxidative stress in the proallergic immunologic effects of particulate and gaseous pollutants. Future therapy to reduce the adverse effects of air pollution on allergic respiratory disease will likely depend on targeting susceptible populations for treatment that reduces oxidative stress, potentially through enhancement of antioxidant defenses (12).

Many different particles and gases are responsible for air pollution. They are divided into six major groups:

1. Carbon Monoxide. This is a colorless, odorless, invisible gas, the product of internal combustion engines. It combines with hemoglobin in red blood cells and displaces oxygen. In small amounts carbon monoxide can cause headaches and fatigue. Large amounts can be lethal.

2. Particulates. This is a general term for a mixture of solid and liquid particles in the air, usually produced by stationary fuel combustion and industrial processes. Particulates include small bits of soot and ashes that emanate from incinerators and smokestacks.

3. Sulfur oxides. These are acrid, corrosive, poisonous gases that come from burning sulfur containing fuel such as coal and oil. They are produced mainly by industrial plants that burn fuel containing sulfur as an impurity.

4. Hydrocarbons. So named because they contain both hydrogen and carbon, these compounds come from the incomplete burning of fuel, mainly gasoline. Although hydrocarbons are not very harmful themselves, they can react with sunlight to form smog, which is irritative. In industrial areas, most hydrocarbons are from automobiles.

5. Nitrogen oxides. These include nitric oxide and nitrogen dioxide (NO_2), produced when fuel is burned at very high temperatures. This occurs mainly in automobiles, electric utilities, metal fabricating plants, and chemical plants. NO_2 is a yellow brown gas that can combine with hydrocarbons and sunlight to form smog and ozone. Ozone is a specific photochemical oxidant that can be irritative to the lungs and eyes.

6. Miscellaneous. A host of other pollutants, including lead, arsenic, asbestos, mercury, beryllium, plutonium, cadmium fluoride, and organic pesticides, may enter the atmosphere from various sources. Airborne lead, mainly from leaded gasoline, has decreased considerably since the conversion by many cars to unleaded gasoline

Smog: There are actually two kinds of smog: photochemical smog due to the action of sunlight on air pollutants, and a combination of smoke and fog (smog) that has nothing to do with sunlight. The original smog, used to

be common when coal was widely used to heat homes. Recently, the term smog used to describe the haze that occurs when sunlight reacts with the hydrocarbons and nitrogen dioxide that are part of automobile exhaust. The reaction of sunlight with hydrocarbons and NO_2 results in a variety of chemical products. One of these is ozone.

Ozone: is a molecule made up of three atoms of oxygen (O_3). Regular oxygen, which of course is vital to life, is a molecule of 2 oxygen atoms (O_2). Adding an extra oxygen atom to form ozone results in an irritative noxious gas. Other undesirable chemicals, such as aldehydes, also result from this photochemical reaction and account for the harmful effects of smog as: eye irritation, cough, and for some, trouble in breathing. Because sunlight is essential to this type of smog, the concentration of ozone and other measurable chemicals is maximum around noon and falls off considerably at night. (13).

Pollution standard index (PSI):

Air pollution, as exists in and around our cities and industrial plants, makes the lives of chronic heart and lung disease patients more difficult. Various local governments now publicize a pollution standard index (PSI) to warn such patients to stay indoors when the air is unsafe (Table 1). The PSI scale ranges from 0 to 500 and is based on the air pollutant with the highest concentration at the time the test is done. Five major pollutants are measured at various points throughout the area: nitrogen dioxide, sulfur dioxide, carbon monoxide, photochemical oxidants (mainly ozone), and particulate matter. The PSI was originally developed by the U. S. Environmental Protection Agency to provide consistency in reporting on air quality. The PSI is published every morning in large city newspapers or is available from the local pollution control agency (14).

Common sense dictates that anyone suffering chronic cardiac or pulmonary disease as asthma, bronchitis, emphysema, cystic fibrosis, coronary artery disease and heart failure, should avoid air pollution to the maximum extent possible, including altering lifestyle, residence, or occupation if necessary and economically feasible.

Effects of community air pollution:

The effects of air pollution should be viewed in two different groups: healthy people and people with chronic heart or lung disease.

Most studies demonstrating harmful air pollution effects have been done on chronic disease patients and the very elderly. It is likely that general air pollution, if severe enough, can also lead to specific diseases in otherwise healthy people. A summary of effects of community air pollution is given in Table 2 (15).

Exposure to Ambient (outdoor) Air Pollution

Ambient (outdoor) air pollution may be deleterious to the health of children with asthma. Airborne allergen is an important cause of exacerbations even in those with intrinsic asthma. It is important to identify the allergens responsible, as some of these may be controllable (16).

II-Effect of air pollution on asthma

Respiratory allergic diseases appear to be increasing in both prevalence and severity in most countries, and subjects living in urban and industrialized areas are more likely to have respiratory allergic symptoms than those living in rural areas. This increase has been linked, among various factors, to air pollution and to the westernized lifestyle. In the outdoor environment, the most important air pollutants are sulphur dioxide, nitrogen dioxide, ozone and particulate matter. Particulate diesel exhaust emissions, besides acting as irritant, are thought to modulate the immune response, with an adjuvant activity on IgE synthesis, thereby facilitating allergic sensitization in predisposed subjects (17). In other words, atopic state can be upregulated by environmental influences, and some subjects develop atopic disease in response to these environmental factors when they are inhaled in combination with aeroallergens. Moreover, air pollutants produce greater responses in asthmatic subjects. Since airborne pollen allergens and air pollutants are often increased contemporaneously, an enhanced IgE-mediated response to aeroallergens and enhanced airway inflammation could account for the increasing frequency of allergic respiratory diseases, in particular those induced by pollen allergens, in urban areas (18).

Some children with asthma (as well as some children without asthma) have decreases in lung function after exposure to ozone (19). Ozone, a pollutant that is formed primarily by vehicular exhaust and is the principal component of urban smog, is associated with

asthma exacerbations in some children with reactive airway disease. Levels of ozone are usually greatest on hot summer days, and the levels tend to reach their peak in the late afternoon. Exposure to ambient sulfur oxides and suspended particulates may also lead to pulmonary function decreases in children.

Nitrogen dioxide is an oxidant gas that can penetrate deep into the lungs and damage delicate lung tissues. Some studies have shown a relationship between nitrogen dioxide and respiratory symptoms.

Shima *et al.* (20) have demonstrated that the prevalence of bronchitis, wheezing, and asthma increased with each increase of 10 parts per billion (ppb) in indoor nitrogen dioxide concentrations among girls but not among boys.

Although ambient air pollution may exacerbate asthma among individual children, a large international study suggests that outdoor air pollution is not a major factor in the development of asthma in populations

Exposure to indoor air pollution

Exposure to indoor air pollutants may have a more important effect on the development of childhood asthma than may exposure to outdoor air pollutants. Many allergens and irritants (from smoke, cockroaches, mites, molds, cats, and dogs) are found indoors. As most people spend the majority of the day (average 20 hours) inside buildings, indoor air pollution has become a particular problem since the energy crisis of the 1970s, which led to the construction of more energy-efficient buildings with less air circulation. The Institute of Medicine recently released a report, *Clearing the Air*, on the relationship between indoor air pollution and asthma (21).

Exposure to Environmental Tobacco Smoke

Exposure to environmental tobacco smoke is a risk factor for the development of asthma and for asthma attacks in children with existing disease. The Institute of Medicine concluded that there is sufficient evidence of an association between exposure to environmental tobacco smoke and the development of asthma and sufficient evidence of a causal relationship between exposure to environmental tobacco smoke and exacerbations of asthma. Exposure to tobacco smoke products in utero is a risk

factor for wheezing in the first year of life. Children who have asthma and whose parents smoke have more frequent asthma attacks and more severe symptoms (21). Moreover, children exposed to maternal smoking had a higher risk of sensitization to house dust mite, especially when the mothers were allergic (22).

Indoor Exposure to Dust Mites

Sensitization to house dust mites is an important risk factor for asthma development and also asthma exacerbations. Household interventions can decrease children's exposure to dust mites. Plastic mattress covers are an effective measure to decrease dust mite infestation of bedding. Several randomized controlled trials have demonstrated a significant decrease in concentrations of mite allergen on mattresses covered by polyurethane casings (23).

Exposure to Cockroaches

Cockroach allergens are causally related to asthma attacks. Cockroach droppings may be one of the most underappreciated allergens in the indoor environment. Multicenter asthma studies funded by the National Institutes of Health have brought to light the importance of cockroach allergens in causing morbidity among inner-city children with asthma. Cockroach allergens not only increase the risk of asthma attacks but also may increase a child's risk of developing asthma (24).

Exposure to Cats

Exposure to cats is causally related to asthma exacerbations among children with asthma (21).

Exposure to Molds

Indoor Exposure

Exposure to molds is associated with asthma exacerbations. Some molds may invoke an allergic response (resulting in asthma or allergic rhinitis) in susceptible children. Exposure to molds may lead to allergic sensitization. At least 60 species of molds have spores thought to be allergenic. Species of particular concern are *Penicillium*, *Aspergillus*, *Cladosporium*, and *Alternaria*. On exposure to these species, nasal congestion, runny nose, sneezing, conjunctivitis, lacrimation, wheezing, chest tightness, and shortness of breath may occur. Thirty percent of patients with respiratory allergies seem to be particularly sensitive to molds. Children are the most sensitive population. Strong associations have been

found between mold or dampness and respiratory symptoms as wheezing, sore throat, and runny nose (25).

Outdoor Exposure

Fungal concentrations in outdoor air vary according to the season and weather conditions. In subarctic climates, patients with mold allergies have more serious symptoms during spring and autumn when outdoor mold concentrations are usually highest. Exposure to environmental molds has been documented to play a role in asthma-related mortality (26).

III-Effect of air pollution on Pulmonary Function

Asthma prevalence is increased in highly polluted districts. PF, FVC, FEV₁, FEF₂₅₋₇₅ all are lowered in highly polluted districts (27). Exposure to high levels of particulate matter with an aerodynamic diameter <2.5 μm (PM_{2.5}) attenuates the protective effect of better lung function against new onset asthma (28). James et al. (29) stated that air pollution have chronic, adverse effects on lung development in children from the age of 10 to 18 years, leading to clinically significant deficits in attained FEV₁ as children reach adulthood. Exposure to ambient air pollution is correlated with significant deficits in respiratory growth leading to clinically important deficits in lung function, showing the importance of lung function as a determinant of morbidity and mortality during adulthood. The specific pollutants that were associated with these deficits included nitrogen dioxide, acid vapor, PM_{2.5}, and elemental carbon. These pollutants are products of primary fuel combustion.

Pulmonary function is variably impaired in response to Ozone exposure. DLCO may drop. Declines in FEV₁ and FVC show great interindividual variability. Laboratory exposures provide the following data (Table 4) but probably underestimate the effects of community exposures (due to interactive effects of other pollutants, allergens, and to other exposure dynamics). While spirometric changes tend to decrease after several sequential days exposure, tolerance does not seem to develop to bronchial hyperresponsiveness. Although ozone has been shown to decrease athletic performance, it has not been shown to exacerbate exercise induced asthma.

Great inter-individual variability exists in ozone responsiveness, with a few individuals

suffering clinically important reactions, most persons experiencing mild responses, with the remainder little affected. Persons at risk include persons with asthma or chronic lung disease, and those who are active outdoors for prolonged periods. Examples of this latter group are athletes, children at play, and outdoor workers such as laborers, policemen and firemen, farmers, linemen, loading dock workers, construction workers, and foresters. Ozone related spirometric compromise is more marked in individuals with chronic obstructive lung disease, than in otherwise healthy smokers. Increasing evidence suggests that asthmatics, after exposure to ozone, have increased bronchial reactivity to subsequent allergens. Some non-asthmatics show a similar pattern. Individual hypersensitivity to specific substances may play a role (30).

Air pollution from road traffic is a serious health hazard, and people with preexisting respiratory disease may be at increased risk **McCreanor et al. (31)**. Efforts for reducing the asthma burden must focus on primary prevention to reduce the level of exposure of individuals and populations to common risk factors, particularly tobacco smoke, frequent lower respiratory infections during childhood, and environmental air pollution (indoor, outdoor, and occupational).

Increasing attention has to be paid to the potential of urban air toxics to exacerbate asthma. Continued emphasis on the identification of strategies for reducing levels of urban air pollutants is warranted to reduce respiratory diseases and other diseases related to pollution.

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0-50	The air is clean and does not pose a serious health hazard.
50-100	Moderate air pollution.
100-200	Unhealthy level; the amount of air pollution may aggravate symptoms in people with underlying heart or lung disease.
200-299	<i>Stage Alert:</i> Very unhealthy elderly people and those with chronic heart or lung disease should stay indoors. Everyone may experience symptoms of lung or eye irritation.
300-399	<i>Second Stage Alert:</i> Anything above 300 is considered very hazardous. All people should avoid outdoor activity.

Table (1): Pollution standard index (PSI) (14)

Known effects
A cause of chronic bronchitis
Exacerbation of chronic bronchitis
Exacerbation of asthma
Exacerbation of emphysema
Impairment of pulmonary function
A cause of cough and other symptoms of respiratory irritation
Contributing factor to excess respiratory deaths in "air pollution disasters"
Possible Effects
A possible cause of emphysema
Weakening defense mechanisms against infection
A cause of lung disease in people who live for many years in the vicinity of manufacturing plants that produce certain products, such as asbestos

Table (2) (15)

Indoor Exposure	Asthma Development	Asthma Exacerbation
House dust mite	Increased	Increased
Environmental tobacco smoke	Probably increased	Increased
Cockroach	Maybe increased	Increased
Cat	Maybe increased	Increased
Dog	Maybe increased	Probably increased
Molds	?	Probably increased
Oxides of nitrogen	?	Probably increased
Ozone	?	Probably increased
Particulates	?	Probably increased
Sulfur dioxide	?	Probably increased

Table (3): Relationship Between Indoor Exposures and Asthma Development and Exacerbations (21).

1 - 2 hours @ 120 ppb	10 - 20 % of population	12% decline FEV1
6.6 hours @ 80 ppb	few individuals	38% decline FEV1
8 hours @ 120 ppb	population average	20% decline FEV1
6.6 hours @ 120 ppb	asthmatics and non-asthmatics	non-specific bronchial hyper responsiveness
1 hour @ 120 ppb	asthmatics	Specific bronchial hyper responsiveness (conflicting evidence)
3 hours @ 250 - 400 ppb	asthmatics	Specific bronchial hyper responsiveness (convincing evidence)

Table (4): Pulmonary function response to various Ozone exposures (30).

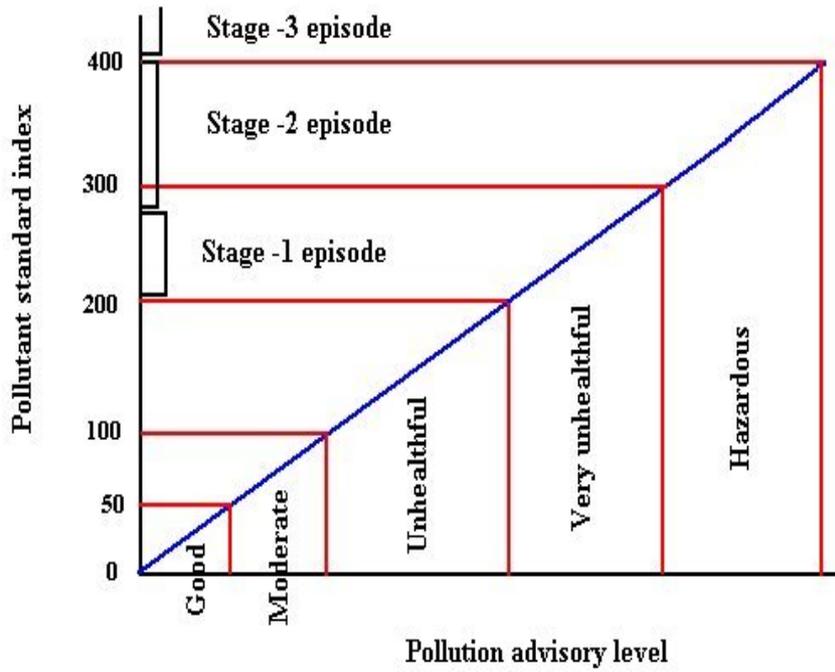


Figure (1): Pollution standard index (15).