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Review

A review on human health perspective of air pollution with respect to allergies and asthma

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ABSTRACT

The increase in cases of asthma and allergies has become an important health issue throughout the globe. Although these ailments were not common diseases a few short decades ago, they are now affecting a large part of the population in many regions. Exposure to environmental (both outdoor and indoor) pollutants may partially account for the prevalence of such diseases. In this review, we provide a multidisciplinary review based on the most up-to-date survey of literature regarding various types of airborne pollutants and their associations with asthma-allergies. The major pollutants in this respect include both chemical (nitrogen dioxide, ozone, sulfur dioxide, particulate matter, and volatile organic compounds) and biophysical parameters (dust mites, pet allergens, and mold). The analysis was extended further to describe the development of these afflictions in the human body and the subsequent impact on health. This publication is organized to offer an overview on the current state of research regarding the significance of air pollution and its linkage with allergy and asthma.

Contents

1. Introduction

The prevalence of allergic diseases has increased around the world in recent decades (Asher et al., 2006; Cakmak et al., 2010; Nicolaou et al., 2005; Solomon, 2011; Szyszkowicz et al., 2009). Since such an increase has taken place in a relatively short period of time, explanations based on genetic changes are insufficient to understand this unique phenomenon (Lobdell et al., 2011). Exposure to environmental pollutants or microorganisms especially in air (both indoors and outdoors) has in fact been identified as the main cause of many common ailments along with allergies (and chemical sensitivities) (Englert, 2004).

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To reduce heating and cooling costs, modern houses are built air-tight with poor ventilation, which can ultimately lead to deterioration in air quality. Under such circumstances, a variety of biophysical pollutants (dust, dirt, lint (from bed sheets), pollen, human skin, and animal dander) can be entrapped and accumulated indoors (Brauer et al., 2007; Solomon, 2011). Dust containing squalene was also reported to contribute to the scavenging removal of ozone in all settings occupied by humans (Charles et al., 2011). Likewise, there is a list of chemical pollutants that are abundant in the outdoor environment (such as volatile organic compounds (VOCs), nitrogen dioxide (NO_2), ozone, etc.), while simultaneously exerting significant influence on indoor air quality (Thurston and Wallace, 2007). If these facilities are not constantly managed against the potentially harmful pollutants, the symptoms of asthma and allergies can worsen (Ring et al., 2001).

This article reviews the common components of indoor pollution that can directly or indirectly induce allergy and asthma. Then, emphasis is put on up-to-date knowledge on the impact of air pollution on those diseases based on evidence collected by the professionals (e.g., hygienists or other environmental health (and safety) professionals) as well as members of the general public suffering from these afflictions. Information presented in this review can thus be used to take appropriate measures against these prevailing diseases.

2. Epidemiological aspects

The development and phenotypic expression of atopic diseases (i.e., allergic rhinitis (hay fever), allergic conjunctivitis, allergic asthma, etc.) depends on a complex interaction between genetic factors, environmental exposure to allergens, and non-specific adjuvant factors such as tobacco smoke, air pollution, and infections (Halken, 2004). The collaborative study known as the International Study on Asthma and Allergies in Childhood (ISAAC) was conducted repetitively using the same methodology with approximately 1.2 million children in 98 countries worldwide (e.g., Mallol et al., 2013). It was reported that the prevalence of symptoms associated with allergic rhinoconjunctivitis ranged from 2.2 to 14.6% among children aged 6–7 years and from 4.5 to 45.5% among adolescents aged 13–14 years during the 12 months prior to the application of the standard questionnaire (Mallol et al., 2013).

The number of people with asthma has grown continuously. In 2011, 235–300 million people worldwide were affected by asthma and allergic rhinitis (World Health Organization(WHO), 2013). One in 12 people (about 25 million or 8% of the U.S. population) had asthma in 2009, compared with 1 in 14 (about 20 million or 7%) in 2001 (CDCP, Centers for Disease Control, Prevention, 2011). In general, such symptoms are reported more frequently in developed than in developing countries (Abdulrahman et al., 2012; Bateman et al., 2008; Wu et al., 2011). Moreover, it is seen more commonly from those who are economically disadvantaged in developed countries, while it is more pronounced in the affluent group in developing countries (Sembajwe et al., 2010). The reason for these differences is not well known. Although asthma is twice as common in boys as girls, severe asthma tends to be found on equal ratio from both sexes (Asher et al., 2006). In contrast, adult women have a higher rate of asthma than men, while the young generation seems to suffer more than the old one (Loerbroks et al., 2012). However, previous studies documented a wide variability in the prevalence and severity of asthma and rhinoconjunctivitis, as observed not between regions and countries but between centers in the same country and centers in the same city. As such, the large variability of these diseases suggests a possibly crucial role of local environment in determining the differences in their prevalence patterns between one place and another.

3. The potent role of chemical pollutants

It is reported that exposure to outdoor airborne pollutants such as ozone (O_3), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and particulates have adverse effects on immune competent cells and airway responsiveness (Delfino et al., 2009; Duki et al., 2003; Jerrett et al., 2005). These outdoor airborne pollutants are known to be released from both mobile (road and off-road vehicles, ships, and aircraft) and stationary sources (power plants, manufacturing industries, waste deposits, agriculture, volcanoes, forest fires, etc.). Many of these chemicals can also be produced indoors, although their concentrations can vary greatly depending on the type of source activities. Moreover, aeroallergens are also carried and delivered by fungal spores or by particles of various origins. In Table 1, the sources of outdoor allergens and their health effects are summarized.

3.1. Ozone (O_3)

As the chief component of urban smog, O_3 is formed by the photochemical reaction in ambient air through interactions with nitrogen oxides and hydrocarbons emitted from traffic and/or industrial sources (U.S. Environmental Protection Agency, U.S. EPA, 2006). Because of the potential to sensitize airway inflammation or damage lung tissues, ozone can cause many types of breathing problems including coughing, wheezing, and chest pain (Szyszkowicz et al., 2012; Trasande and Thurston, 2005; Xu et al., 2011). It can also increase the immune response to allergens in some individuals (Auten and Foster, 2011). Approximately 40–60% of inhaled O_3 is absorbed in the nasal airways, while the remainder can reach the lower airways (Bosson et al., 2008). Bayram et al. (2001) demonstrated that O_3 and NO_2 modulate airway inflammation, while stimulating the release of inflammatory mediators from bronchial epithelial cells. Moreover, O_3 can also prompt a dose-dependent increase in

Table 1
Chemical pollutants and their impact on allergy and asthma.

Order	Pollutants	Source	Health effect	Reference
1	Nitrogen dioxide	Vehicle exhaust, power plants, gas cooking stoves, kerosene space heaters, and other sources that burn fossil fuels	Chronic and acute changes in lung function, bronchial neutrophilic infiltration, proinflammatory cytokine production, and response to inhaled allergens in subjects with asthma	Koenig, 1999; Barck et al., 2005; Everard, 2006
2	Ozone	Photochemical reaction involving ultraviolet radiation acting upon atmospheric mixture of nitrogen oxides and hydrocarbons emitted from vehicles and/or industrial sources	Inhalation of ozone at high concentration increase risk of asthma development, airway inflammation, and responsiveness	Bell et al., 2004; Auten and Foster, 2011
3	Sulphur dioxide	Industrial activities following the combustion of coal and oil	Sulphur dioxide can induce acute constriction of the bronchi to asthmatic patients. It can induce the development of asthma	Winterton et al., 2001; Brown et al., 2003
4	Particulate matter	Natural sources such as dust storms, vegetation, and/or anthropogenic sources like industry and vehicle emissions	Increases the number and severity of asthma attacks, bronchitis and other lung diseases may aggravate due to the penetration of particulate matter	Trasande and Thurston, 2005; Porter et al., 2007
5	Volatile organic compounds	Vegetation, automobile emissions, gasoline marketing and storage tanks, petroleum and chemical industries, dry cleaning, natural gas combustion, etc.	Respiratory, allergic, or immune effects in infants or children, nocturnal breathlessness, increased bronchial responsiveness, and decreased lung function	Delfino et al., 2003; Rumchev et al., 2004

Table 2
Ozone concentrations and associated adverse health effects in healthy individuals.

Order	Concentration (ppm)	Exposure duration and activity	Health effect	Reference
1	0.08	6.6 hours moderate exercise	Respiratory symptoms, increases in nonspecific airways Responsiveness, Increases in lung lavage protein content and polymorphonuclear cells	Bell et al., 2004
2	0.12	1–3 h heavy exercise	Cough	Auten and Foster, 2011
3	0.12	8 hour moderate exercise	Temporary moderate lung Function impairment in 50% of individuals exposed	Bell et al., 2004
4	0.12	8 hour moderate exercise	Temporary large lung function Impairment in 20% of Individuals exposed	Bosson et al., 2008
5	0.12	8 h moderate exercise	Temporary moderate to severe Respiratory symptoms in 10–15% of individuals exposed	Auten and Foster, 2011
6	0.16 –0.18	1–3 h heavy exercise	Shortness of breath, chest pain on deep inspiration, lower respiratory scores	Bell et al., 2004
7	0.18	1–3 h heavy exercise	Increase in nonspecific airways responsiveness	Auten and Foster, 2011
8	0.40	1–3 h rest	Increase in nonspecific airways responsiveness	Auten and Foster, 2011

intracellular reactive oxygen species and in epithelial cell permeability. Inhaled allergens and toxins may then activate the release of inflammatory cells and their products (interleukin (IL)-1, -6, -8, tumour necrosis factor, etc.) (Auten and Foster, 2011; Bell et al., 2004).

In Table 2, ozone concentration levels are summarized briefly in relation to the associated health effects. The effect of ozone exposure has been investigated under the high (0.4 ppm) (Kreit et al., 1989) and low (0.16 ppm) levels for a prolonged duration (7.6 h) (Horstman et al., 1995). The results consistently showed sensitive responses in asthmatic subjects relative to healthy controls. Halonen et al. (2008) also documented increased hospital admissions (or emergency department visits) of respiratory disease patients (e.g., asthma) after inhalation of enhanced O_3 levels (0.11 ppm) in ambient air. A survey of more than 70,000 children in Turkey, aged from 3 to 17, revealed that asthmatic subjects, when exposed to O_3 (50 to 100 ppb) and NO_2 (200 to 400 ppb), exhibited a significant increase in the release of IL-8, GM-CSF, RANTES, and sICAM-1 after 24 hours of incubation (Bayram et al., 2001).

Molfino et al. (1991) reported that 1 hour of exposure to 0.12 ppm O_3 made a two-fold reduction in the provocation concentration of inhaled antigen, causing early bronchoconstriction in specifically sensitized asthmatic subjects. Under the same exposure conditions, the mean provocation dose of ragweed necessary to reduce "forced expiratory volume in one second (FEV1)" by 20% in such subjects was reduced to approximately one-half the dose of the allergen. Jorres et al. (1996) investigated the effect of ozone exposure (0.25 ppm) through a mouthpiece with intermittent exercise over a longer duration (3 hr). They found that 23 out of 24 mild asthmatic subjects experienced a 20% decrease in FEV1 at a lower provocation dose of allergen. Likewise, Peden et al. (1995) reported enhanced nasal inflammatory responses to local allergen challenge after O_3 exposure to subjects with allergic rhinitis. According to Hwang and Jaakkola (2008), co-exposure to O_3 and NO_2 significantly promoted the allergen-induced release of eosinophil cationic protein in nasal lavage.

3.2. Nitrogen dioxide (NO_2)

NO_2, a precursor of photochemical smog, can be found ubiquitously in both indoor and outdoor air (Berhane et al., 2011; Bevelander et al., 2007; Latza et al., 2009; Shima and Adachi, 2000). Emissions from automobile exhaust, power plants, and fossil fuels are the pivotal sources of outdoor NO_2, while gas cooking stoves and kerosene space heaters are frequent indoor sources. NO_2 exposure can induce chronic and acute changes in lung function, including bronchial neutrophilic infiltration, proinflammatory cytokine production, and responses to inhaled allergens in subjects with asthma, both alone and with sulfur dioxide (Barck et al., 2005; Delfino et al., 2006; Everard, 2006; Koenig, 1999; Kraft et al., 2005). Inhalation of NO_2 is injurious to the lung, and it can augment the degree of allergic airway inflammation and prolong allergen-induced airway hyperresponsiveness in rodent models of asthma (Poynter et al., 2006).

In Table 3, effects of nitrogen dioxide on those suffering from pre-existing disease are summarized. As NO_2 can be absorbed all along the respiratory tract, injury can be found in the trachea, bronchi, bronchioles, alveolar ducts, and the proximal airways, depending on

Table 3
Controlled studies of the effects of nitrogen dioxide in patients with pre-existing diseases.

Order	Concentration (ppm)	Exposure duration and activity	Effect	Reference
1	0.10	1 h	No effect on specific airway conductance or FEV1, or reactivity to ragweed; variable effect (nonsignificant trend) on carbachol reactivity	Bevelander et al., 2007
2	0.15	1 h	No change in specific airway resistance or grass pollen reactivity in three allergic asthmatics and four allergic Subjects	Bevelander et al., 2007
3	0.20	2 h (1 h of exercise at 20 l/min)	No effects on spirometry or specific airway resistance; variable increase in methacholine reactivity	Kraft et al., 2005
4	0.30	1 h (30 min of exercise at 41 l/min)	No effects on function or reactivity to cold air	Persinger et al., 2002
5	0.30	2 h (1 h of exercise at 40–41 l/min)	No significant effects on specific airway resistance	Bevelander et al., 2007
6	0.50	2 h (15 min of exercise at 25 l/min)	No effects on bronchitis alone; possible decrease in quasistatic compliance	Chen et al., 2007
7	1.0	1 h	No effects on function or reactivity to cold air	Persinger et al., 2002
8	5.0	1 h	Decreased partial pressure of oxygen	Persinger et al., 2002

its concentration and dose (Berhane et al., 2011). Poynter et al. (2006) demonstrated that 0.1 to 0.6 ppm of NO_2 is sufficient to induce airway hyperresponsiveness (AHR), a hallmark feature of allergic airways disease. Moreover, they demonstrated that NO_2 is apt to augment and prolong ovalbumin induced inflammation and AHR. As such, NO_2 can act as an important mediator contributing to the pathological effects in the allergic inflamed lungs. Belanger et al. (2006) conducted a controlled human-exposure study in which all eight asthmatic subjects experienced increased allergen-induced early bronchoconstrictor responses after exposure to 0.4 ppm NO_2 for 1 hr. Bevelander et al. (2007) also found that exposure to 10 ppm NO_2 (over 1 hr duration) increased bronchoalveolar lavage fluid levels of total protein, lactate dehydrogenase activity, and heat shock protein (Hsp70s), which could activate NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells). These findings can offer insight into a mechanism through which allergen sensitization may develop under ambient (or endogenous) conditions at high NO_2 levels. Hesterberg et al. (2009) conducted more than 50 experimental studies with respect to human inhalation of NO_2. These authors concluded that NO_2 induced lung inflammation is not expected to occur below 0.6 ppm for asthmatics and individuals with chronic obstructive pulmonary disease (COPD). However, some sensitive subsets may respond to levels as low as 0.2 ppm.

3.3. Sulfur dioxide

SO_2 is released primarily from the combustion of sulfur-containing coal and oil. People prone to allergies, especially allergic asthma, can be extremely sensitive to inhaled sulfur dioxide. Symptoms may include bronchospasm, hives, gastrointestinal disorders, and inflammation of the blood vessels (vasculitis-related disorder) (ATSDR, Agency for Toxic Substances, Disease Registry, 2007; CARB, California Air Resources Board, 2009; U.S. Environmental Protection Agency, U.S. EPA, 2010).

Table 4 lists the health effects associated with respiratory exposure to sulfur dioxide. The concentration of SO_2 (0.3 to 0.6 ppm) needed to induce acute bronchoconstriction in asthmatic subjects is much lower than those of healthy subjects (Brown et al., 2003). Unlike O_3, the bronchoconstrictor effect of inhaled SO_2 on asthma patients proceeds imminently (Frampton and Utell, 2007). According to Meng et al. (2003), 10 min exposure to 0.5 ppm SO_2 was sufficient to induce a rapid-onset of bronchoconstriction (decreases in FEV_1 or increases in airway resistance within 2 min) in both healthy and asthmatic subjects. In response to the inhalation of SO_2 (e.g., 0.25 ppm), asthmatic subjects experienced pronounced symptoms of reduced pulmonary function relative to nonasthmatic subjects who were often unresponsive at less than 5 ppm (Meng et al., 2003). In another study, the TNF-α promoter polymorphism was identified in asthmatic patients who were exposed to 0.5 ppm of SO_2 for 10 minutes (Winterton et al., 2001). As ambient SO_2 can contribute to the formation of acid aerosol (H_2SO_4), some studies suggested the possibility of increasing asthma symptoms on days with highly acidic aerosols (U.S. Environmental Protection Agency, U.S. EPA, 2008). In Washington, USA, Bateson and Schwartz (2008) in fact observed increased hospital admissions of very young asthma patients with enhanced SO_2 exposure.

3.4. Particulate matter

Particulate matter (PM) is a heterogeneous mixture of particles consisting of dirt, soot, smoke, and even liquid droplets (aerosols) emitted from diverse natural and anthropogenic sources, e.g., factory smokestacks, diesel-powered engines, as well as power generation, construction, mining, and agricultural activities (Chen et al., 2008; Rosenlund et al., 2009, 2011; Son et al., 2011). As the particles can easily penetrate deeply into lungs, they increase the frequency and severity of asthma attacks. The penetration of PM can thus aggravate bronchitis and other lung diseases while reducing the body's ability to fight infections (Trasande and Thurston, 2005). In animal experiments, the contamination status of PM-bound transition metals (e.g., chromium, cobalt, copper, manganese, nickel, titanium, vanadium, zinc, etc.) was strongly correlated with the extent of radical activation and lung injury (Kleinman et al., 2007).

Health effects of PM exposure are summarized in Table 5. In a study conducted in Turkey, Tecer et al. (2008) demonstrated that children with atopy and bronchial hyperresponsiveness were at a high risk of such symptoms during episodes of high PM pollution. They also found that for every 100 $\mu g\text{-}m^{-3}$ increase in PM, respiratory symptoms in children (with bronchial hyper-responsiveness and high levels of serum total immunoglobulin (Ig)E) increased by as much as 139%. Likewise, healthy volunteers exposed to diesel exhaust particulate (DEP) in 400 to 600 $\mu g\ m^{-3}$ levels were seen to have a greater number of alveolar macrophages, neutrophils, and T-lymphocytes in bronchoalveolar lavage fluid (BALF) than the control group (Porter et al., 2007). Ito et al. (2011) observed that DEP and ragweed allergen challenge markedly enhanced human in vivo nasal ragweed-specific IgE and skews cytokine production to a T-helper cell type-2 (Th2) pattern. Moreover, there is evidence that increases in PM levels played a key role in the enhancement of allergic inflammatory response leading to eosinophilic inflammation and mucoid hyperplasia starting at the nasal turbinates all the way down to the small pulmonary airways (Lee et al., 2007; Pope and Dockery, 2006). In the review of experimental studies conducted on animals and humans, Li et al. (2009) showed that DEPs should enhance IgE production by a variety of mechanisms, including the effects on cytokine and chemokine production, as well as activation of macrophages and other mucosal cell types. Because PM can also absorb aeroallergens released by pollen grains, it can contribute to an enhanced IgE mediated response with the prolonged retention of the allergen (Zhou et al., 2011).

3.5. Volatile organic compounds (VOCs)

Many VOCs constitute the key components of various materials used in the livelihood facilities such as interior furnishings, textiles, office equipment, cleaners, personal care supplies, and pesticides (Uhde and Salthamme, 2007). For instance, acute effects are known to occur by exposure to VOCs due to the use of diverse spray products that generally contain various types of VOCs. Specifically Zock et al. (2007) found that the frequent use of household cleaning sprays known to emit various VOCs types can lead to a 40% increase in wheeze and a 50% increase in asthma symptoms. As such, exposure to VOCs has been designated as

Table 4
Health effects of respiratory exposure to sulfur dioxide.

Order	Concentration (ppm)	Health effect	Reference
1	1–5	Threshold for respiratory response in healthy individuals upon exercise or deep breathing	Frampton et al., 2007
2	3–5	Decrease in lung function at rest and increased airway resistance	Meng et al., 2003
3	5	Increased airway resistance in healthy individuals, irritation of eyes, nose and throat	Brown et al., 2003
4	10	Upper respiratory irritation, some nose bleeds	Brown et al., 2003
5	10–15	Threshold of toxicity for prolonged exposure	Frampton et al., 2007
6	20	Paralysis or death after extended exposure	Brown et al., 2003
7	150	Maximum concentration that can be withstood for a few minutes by healthy individuals	Szyszkowicz et al., 2009

Table 5
Health effects to exposure to airborne particular matter.

Order	Concentration (μg g m^{-3})	Health effects	Reference
1	Increases of 10 μg m^{-3} of PM in same day	1.9% and 3.3% respective increases in respiratory and cardiac hospital admission	Kleinman et al., 2007
2	Increases of 20 μg m^{-3} of PM in same day	8% increase of lower respiratory illness among children	Kleinman et al., 2007
3	120	Increase in hospital admissions of children with respiratory disease	Tecer et al., 2008
4	150	Increase the likelihood of respiratory symptoms and aggravation of lung disease	Rosenlund et al., 2009
5	200	Increase in respiratory diseases such as pneumonia, chronic obstructive pulmonary disease (COPD), and asthma	Rosenlund et al., 2011
6	400 to 600	Alveolar macrophages, neutrophils, and T-lymphocytes in bronchoalveolar lavage fluid	Porter et al., 2007

the primary suspect causing a number of asthma and asthmatic symptoms including breathlessness, increased bronchial responsiveness, and suppressed lung function (Rumchev et al., 2004).

The concentration levels of VOCs that can affect human health are summarized in Table 6. Ware (2003) reported an association between ambient concentrations of VOCs (2 mg m^{-3}) and asthma in children with 7–13 years of age. In other studies, VOCs were also seen to induce inflammation and airway obstruction (Delfino et al., 2003; Pappas et al., 2000; Rumchev et al., 2004). Likewise, many authors observed the development of moderate to strong symptoms in respiratory and allergic problems among children exposed to relatively high concentrations (20 to 50 μg m^{-3}) of VOCs (including formaldehyde) (e.g., Mendell, 2007). In a review made by the California EPA (2007), a linkage of formaldehyde with increases in asthma-like respiratory symptoms is identified based on a line of evidence supported by chamber exposure and animal studies on the toxicological mechanisms.

4. Biophysical parameters in the indoor environment

The predominant fraction of indoor pollutants of biophysical origin (e.g., dust mite allergens, pet allergens, mold, etc.) in general acts as irritants. Moreover, they can also expand allergic reactions to indoor allergens, making symptoms worse. The sources and effects of such allergen in the indoor environment are listed in Table 7.

4.1. Dust mite allergens

Dust mites are spider-like microscopic insects that can travel through the air (Zhao et al., 2009). They feed off dead skin cells from humans and often become a major component of indoor dust. Dust mites, like other biological contaminants, contribute to poor indoor air quality (IAQ). They can trigger allergic reactions and cause rashes, watery eyes, coughing, dizziness, lethargy, breathing difficulties, and digestive problems (Jiang et al., 2009). House dust mite allergens are also known to play an important role in inducing IgE-mediated sensitization and the development of bronchial hyperresponsiveness (BHR) and asthma (Glasgow et al., 2011).

Exposure to dust mite allergen, especially in atopic children, was ascribed to the sensitization to the allergen (Lau et al., 2000), while such sensitization was pointed out as a major independent risk factor for asthma (Mihrshahi et al., 2003). Dust mite allergen concentration of 10 μg g^{-1} was in fact proposed as exposure thresholds for the development of allergic sensitization and asthma (Trombone et al., 2002). However, there is also contrasting evidence that sensitization may occur at much reduced concentrations (Ghaemmaghami and Shakib, 2002).

Liu et al. (2005) found a strong correlation between wheezing and sensitization to the house-dust mite in a study conducted in Tainan, Taiwan. In another study, a modest correlation was found between hyperresponsiveness and individuals exposed to house dust mites ($r = 0.23, p < 0.03$) (Sharma et al., 2009). Their findings also supported the idea that house dust mite allergens should be an important cause of childhood asthma. Hammad et al. (2009) reported that house dust mite allergen induced asthma via TLR4 triggering airway structural cells. Sporik et al. (1993) found that a majority of children (63 out of 82) exposed to house dust mite allergens were admitted to hospitals with exacerbated asthma. The mean concentrations of mite allergens between different kinds of indoor sources are listed in Table 8.

4.2. Pet allergens

Allergies to pets are common, especially among people who have other allergies or asthma. It has been estimated that 10 percent of the population are allergic to animals (Sharif et al., 2004), while 20 to 30 percent of asthma patients have pet allergy symptoms (Sharif et al., 2004). Pets can cause problems for allergic patients in several ways. Pet dander, skin flakes as well as saliva and urine can cause an allergic reaction (Woodcock et al., 2001). Although animal hair (or fur) is not considered a very significant allergen, it can also act as a media to transmit pollen, dust, mold, and other allergens (Woodcock et al., 2001).

The most common household pets are dogs, cats, birds, hamsters, rabbits, mice, gerbils, rats, and guinea pigs. Cat allergies are about twice more common than dog allergies (Woodcock et al., 2001). A possible explanation is that inhalation of high levels of the major cat

Table 6
Associations between the measured indoor VOC concentrations and their health effects.

Order	Pollutants	Concentration (μg m^{-3})	Health effect	Reference
1	Total VOCs	393	Persistent wheezing	Venn et al., 2003
2	Sum of 10 VOCs	Aromatics, 78.5 (median)	Diagnosed asthma; peak expiratory flow; respiratory symptoms	Rumchev et al., 2004
3	Sum of 26 VOCs	Alkanes and aromatics, 89.3; Terpenes 562; limonene, 19.1 benzene 1.70; toluene 13.3	Increased IgE sensitization to foods; elevated total IgE; Producing CD8 + T cells; Reduced proportion of CD8 + IL-4 producing T cells	Lehmann et al., 2001
4	Sum of 28 VOCs	Alkanes 16; Aromatics 98; Terpenes 198	Producing type 1 T cells in cord blood; Elevated proportion of IL-4-producing type 2 T cells in cord blood	Lehmann et al., 2002

Table 7
Types of biophysical pollutants and their impact on allergies.

Order	Pollutants	Source	Health effect	Reference
1	Dust mites	Mattresses, pillows, bedcovers, carpets, upholstered furniture, stuffed toys, and other fabric items	Exacerbate allergic rhinitis, atopic dermatitis, IgE-mediated sensitization, bronchial hyperresponsiveness (BHR) and asthma	Ghaemmaghami and Shakib, 2002; Glasgow et al., 2011
2	Pet allergens	Pet animals with fur	Trigger severe asthma attacks, may cause acute symptoms of allergic conjunctivitis, inflammation of the eye, and hay fever	Blay et al., 2002; Sharif et al., 2004
3	Mold	Damp or wet building materials and furnishings, any source of moisture	Nasal stuffiness, eye irritation, wheezing, skin irritation, allergic reactions, trigger asthma attacks	O'Hollaren et al., 1991; Custovic and Woodcock, 2000

allergen *Fel d* 1 induces the production of IgG and IgG4 antibodies with a protective effect (Leaderer et al., 2002). For about 20 to 30 percent of people with asthma, cat contact can trigger a severe asthma attack (Leaderer et al., 2002). However, dogs have been reported to cause acute symptoms of allergic conjunctivitis, inflammation of the eye, and hay fever, when coming in contact with their owners after running through fields (Blay et al., 2002). If a comparison is made by particle size, the predominant fraction (~80%) of the allergenic material from dogs (Can f 1) and cats (Fel d 1) are found on particles >5 μm (Custovic and Chapman, 1997) and <5 μm (Custovic et al., 1998), respectively. Fel d 1 is a serious cause of asthma in sensitized individuals (DeMartino and Passalacqua, 2003). In industrialized countries, up to 40% of adults or children (2–4 years of age) with atopy and asthma were estimated to be sensitized to Fel d 1(Samoli et al., 2011). Lau et al. (2000) tracked 939 children (from birth to 7 years of age) to explain the relationship between early pet exposure and the prevalence of asthma. Perzanowski et al. (2002) suggested that many of the children exposed to domestic cats can develop an immune response that does not include immunoglobulin E. They also observed suppressed protective trends with dog ownership.

According to Brunekreef et al. (2004), selective avoidance and removal of pets led to distortions of cross-sectional associations between pet ownership and respiratory allergies (and disease) among children. In a nationally representative survey at 831 US homes, geometric mean concentrations (μg/g) of Can f 1 and Fel d 1 were found to be 4.69 and 4.73, respectively. Among homes owning dogs and cats, geometric mean concentrations (μg/g) were 69 and 200, respectively (Arbes et al., 2004). However, Can f 1 and Fel d 1 are present ubiquitously in US homes. Their concentration levels, known for an increased risk of allergic sensitization, were also found in homes without pets. This observation also implicates the possibility of the transportability of these allergens by the community (e.g., on clothing) (Arbes et al., 2004).

Custovic et al. (2003) investigated the relationship between exposure to dust mites and cat and dog allergens using dust sampling and skin prick tests in a large sample of 2502 adults. They concluded that sensitization rates to dust mites might rise, if the rates of concurrent combined exposure increase. However, cat ownership was associated with a lower prevalence of sensitization to cats and dogs but not to mites and grass pollen (Custovic et al., 2003). The influence of indoor levels of house dust mite allergen and cat allergen on sensitization was investigated in another study of 485 adults in Melbourne, Australia (Dharmage et al., 2001). Their findings suggest that the results may be changeable depending on the studied population, the study design, and statistical methods. Consequently, a large scale, longitudinal study will be required to properly assess the cause-and-effect relationship between exposure and sensitization to indoor allergens.

Campo et al. (2006) assessed the relationships between early pet ownership and endotoxin exposure with atopy and wheezing during infancy. They found that high endotoxin exposure in the presence of multiple dogs was associated with reduced wheezing. Hodson et al. (1999) found that washing could significantly reduce recoverable Can f 1 from clippings (84% reduction: from 73 mg/g to 12 mg/g (geometric mean); $P < 0.0001$) and from dander samples (86% reduction: from 347 mg/g to 50 mg/g (geometric mean); $P < 0.0001$). In another study, a significant improvement in airway hyperresponsiveness and a decrease in peak flow amplitude were observed by the application of air cleaners for young asthmatic patients sensitized and exposed to pets in the home (Heide et al., 1999).

Table 8
Mean concentration of mite allergens under different kinds of indoor source conditions.

Order	Source	Mean concentration (μg g^{-1})	Reference
1	Carpeting	1.30	Arbes et al., 2003
"	Stuffed toys	1.42	Arbes et al., 2003
3	Mattresses	14.3	Jooma et al., 2005
		19.6	Radon et al., 2000
		22.2	Mihrshahi et al., 2003
		23.3	Rijssenbeek-Nouwens et al., 2002
		22.3	Tobias et al., 2004
		18.5	Neffen et al., 1996
4	Pillows	24.1	Tobias et al., 2004
		21.4	Neffen et al., 1996

4.3. Mold

Mold is a saprophytic fungus to which certain individuals exhibit a sensitive response (World Health Organization, WHO, 2009). A host of studies have been conducted to assess the prevalence of molds in typical, clean homes. Burge et al. (2005) reported that median levels of fungi in carpets ranged from 10,000 to 100,000 colony forming units per gram (CFU $g^{-1)}$ of material. In another large-scale study, a total of 243 bulk samples were collected from 30 problematic buildings and 5 control (clean) buildings (Scott and Hodgson, 1998). The average concentrations of fungi in the carpets of those buildings were found at 1,844,000 and 30,256 CFU g^{-1}, respectively. However, a medical organization reported that indoor molds, compared to outdoor molds, were considered to comprise only a minor fraction, despite their importance in the development of allergic airway diseases (Hardin et al., 2002). In a review by Horner et al. (1995), indoor exposures to cats, dust mites, and cockroaches were suggested to cause more health problems than indoor molds.

In another study of 11 patients (age range 11 to 25 years) in Minnesota, USA, O'Hollaren et al. (1991) found that exposure to molds can cause symptoms such as nasal stuffiness, eye irritation, wheezing, and skin irritation. Molds, particularly their spores, are apt to produce allergenic and toxic materials in the form of mycotoxins and glucans (Gots and Pirages, 2002). The National Academy of Sciences (NAS), USA (2000) found sufficient evidence linking fungal exposure and symptom exacerbation in sensitized asthmatics. Dharmage et al. (2002) studied the effect of seasonal fluctuations in indoor mold levels and concluded that the mold exerts adverse effects on asthma, regardless of season. Mold exposure may also be related to non-specific chest problems. Custovic and Woodcock (2000) found that the mold genus Alternaria affected asthma significantly based on a skin prick test. Ross et al. (2000) also reported a possible connection between molds and emergency treatments. Likewise, Dales et al. (2000) also found such association in a quantified study. In a meta-analysis, Fung and Hughson (2002) concluded that there is a possible interactive

relationship between mold, allergy, and respiratory symptoms. However, evidence is yet inadequate (or insufficient) to support the direct linkage between fungal exposure and the asthma development. Pirages (2003) stated that mold concentrations commonly found in homes are yet insufficient to account for any negative health effects. As such, the mold study group of Institute of Medicine (IOM), USA was unable to provide reliable evidence in line with the argument that the normal presence of mold in residences and workplaces did not cause any adverse health effects (IOM, Institute of Medicine, 2004).

5. Development of allergies and asthma in human body

An allergic reaction occurs when the human immune system reacts to a foreign substance from the outside world. The most common foreign substances may include molds, dust mites, animal dander, chemicals, foods, insect stings, etc. (Bjorksten, 2004). The immune system responds to these foreign substances that can act as potentially dangerous invaders by sending out antibodies (e.g., immunoglobulin E (IgE)) to attack them. These foreign substances are referred to as allergens and individuals will experience the symptoms of an allergic reaction (Bisgaard et al., 2011). Symptoms of allergies include sneezing, runny nose, sore eyes, itchy throat, eczema, and certain other irritating skin conditions (D'Amato et al., 2002; Szyszkowicz et al., 2009).

Allergies can affect anyone, regardless of age, gender, race, or socioeconomic status. Although the exact genetic factors are not yet understood, the susceptibility to allergies and related diseases is linked to heredity (Brauer et al., 2007). Allergy shots are also an effective and safe treatment for people who suffer from a variety of allergic diseases, including allergic rhinitis (hay fever) and asthma (Ring et al., 2001). The treatment may work, if small amounts of purified substances are introduced to what causes allergy with gradual increments of dosage on a regularly scheduled basis. Allergy shots improve the patient's natural resistance to the particular allergens via the production of blocking antibodies (called IgG antibodies) and a decrease in the level of allergic or IgE-mediated antibodies (Ring et al., 2001; Ruokonen et al., 2010; Saporta, 2012). Fig. 1 shows the mechanism of allergic reaction in humans.

Scientists have characterized asthma as a special type of inflammation of the airways leading to the contraction of airway muscled, mucus production, and swelling in the airways (Apter, 2011; Barnes, 2012; Jackson et al., 2011). As the airways become overly responsive to environmental changes, the result is wheezing and coughing (Jackson et al., 2011). Inflammation of the lining of the airways is a

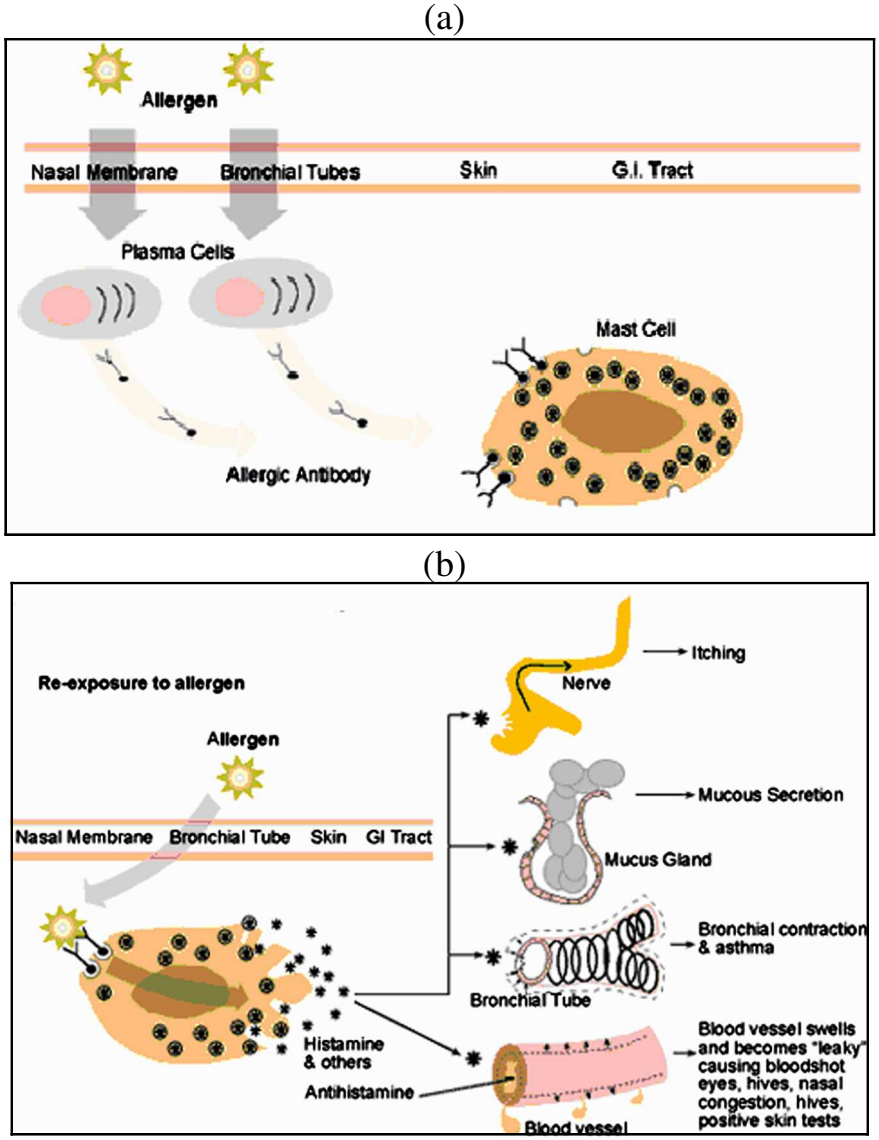

Fig. 1. Development mechanism of allergic reactions in human (a) allergic sensitization and (b) allergic reaction (Source: Zuercher et al., 2006).

major factor in asthma. Inflammation is produced by the human immune system. The immune system's job is to defend our body against impurities with foreign and harmful bacteria, viruses, dust, chemicals, etc. (Marra et al., 2006). The immune system in people with asthma however overreacts by releasing many different kinds of cells and other chemicals to the airways (Holgate, 2011). These cells cause the following changes in the airways: (1) swell or inflame (inflammation) the inner linings of the airways with less room in the airways to transmit the air, (2) tighten the muscles surrounding the airways which narrows the airways even more, and (3) produce thick mucus from the mucus glands in the airways, which further blocks the airways (Apter, 2011). The effect of asthma on bronchial airways is shown in Fig. 2.

Although scientists are yet unable to identify the cause of different asthma types, it is suspected that many different genetic and environmental factors play a role (Masoli et al., 2004). Probably the most important factor in the development of asthma is atopy (Szefler, 2011). Exposure to certain allergens (e.g., house dust mites, cat dander, cockroach droppings, mold, etc.) in early childhood may also play an important role in the development of asthma (Masoli et al., 2004).

The symptoms of asthma include coughing, tight chest, wheezing, and shortness of breath (Sennhauser et al., 2005). Both the frequency and severity of asthma symptoms can be reduced by the use of medications and by reducing exposure to the environmental triggers of asthma attacks (Szefler, 2011). Nevertheless, medical research found that children exposed to certain types of infections during their first year or two of life may be less likely to develop asthma (Clark et al., 2010). For example, these authors indicated that many children growing up on or near farms and exposed to livestock and poultry are less likely to develop asthma and allergies (Selgrade et al., 2006). The same appeared to be true of children who have two or more older siblings or attend daycare during their first 6 months (Selgrade et al., 2006). This possibly reflects the fact that children who are around numerous other children or animals in early life are exposed to more microbes; their immune systems are however likely to gain greater tolerance to more effectively compete with the potential asthma irritants than children without such exposure (Fishbein and Fuleihan, 2012; Koloski et al., 2008).

Asthma is a chronic disease to be cared for all time instead of when symptoms are present. Air pollution (e.g., pollen, dust, and chemicals) and physical activity are all common triggers of asthma (Apter, 2011). Although the treatment of this disease may not be simple or effective, one can rely on dehumidifiers (or air purifiers) to control indoor air quality or have a series of vaccinations (Bolton et al., 2012). Basically, maintenance of good air quality at home should be the key component of asthma management. Irritants such as tobacco or wood smoke, perfumes, aerosol sprays, cleaning products, and fumes from paint or cooking gas can flare-up such symptoms without warning (Chang, 2011). Even scented candles or fresh newsprint can be the causes of recurring asthma for some people (Bernstein et al., 2008). To maintain good air quality inside home, one needs to refrain from smoking inside the house and avoid wood fires, scented products (e.g., scented candles), or room fresheners. Gas fireplaces and stoves should be checked and serviced regularly to prevent gas leaks. The use of unscented or nonaerosol forms of laundry detergent and cleaning products is also recommended. The air conditioning system should run, especially on days with high pollen (or mold) counts and ozone pollution warnings. In addition, the air conditioning filter should be changed on a regular basis. Windows should be opened after midmorning, as pollen counts tend to rise from 5 AM to 10 AM (Sharma et al., 2009).

6. Health effect of allergy and asthma

The presence of airborne pollutants has been identified as the primary cause of allergic symptoms in predisposed subjects (Bernstein et al., 2008; Rosenlund et al., 2009). There is also evidence that airway mucosal damage and impaired mucociliary clearance induced by air pollution may facilitate the penetration and access of inhaled allergens to the cells of the immune system (Yang and Chen, 2007). One of the most dangerous allergic responses is chronic inflammation, which can cumulatively damage tissue wherever it occurs (Zheng et al., 2011). In such instances, antibodies attack the intruder, and this process draws other tissues, cells, and fluids to the afflicted area (Guo et al., 2007). As the genetic predisposition to producing the IgE antibody in response to allergens, atopy increases the risk of developing allergic disorders (Bielory and Friedlaender, 2008). If such a disorder occurs, it can significantly increase the risk of developing other allergic disorders (Murray et al., 2011). Beyond acute symptoms, there are also both short and long-term dangers. Repeated allergic reactions in certain areas of the body can result in damaged organs (Meltzer et al., 2009; Nagata et

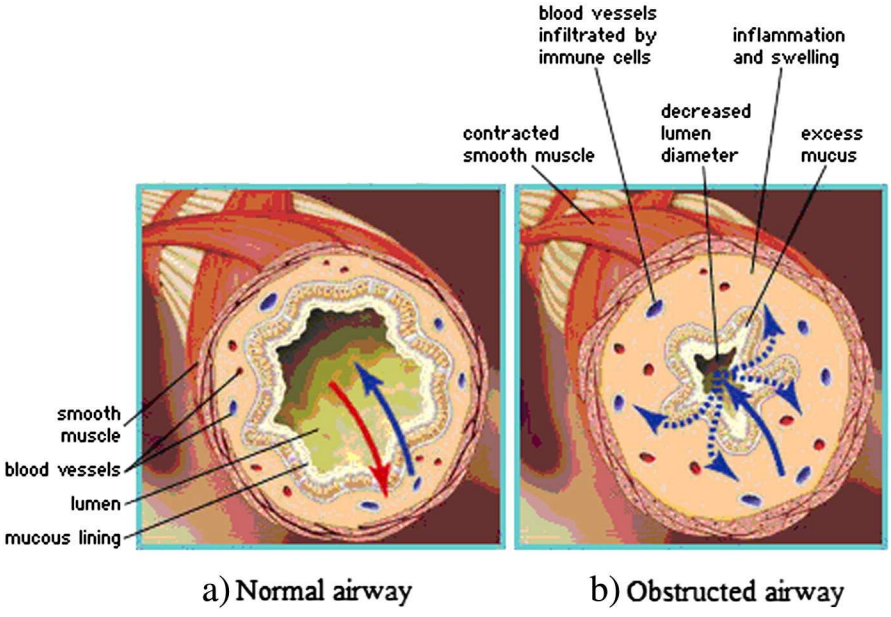

Fig. 2. Effect of asthma on bronchial airways (Source: Apter, 2011).

al., 2010). Asthma, for example, can lead to irreversible emphysema (Simpson et al., 2008). Moreover, an allergy can cause a reaction that leads the blood vessels to dilate and the airways to constrict, making breathing harder. This situation can induce an anaphlyactic shock, which could ultimately result in death (Spergel, 2010).

Although it is not common, there have been many incidences of death during asthma attacks depending on the length and intensity (Asher et al., 2006). The major threat to an asthma sufferer is permanent lung damage (Bousquet et al., 2008). This long-term lung damage actually increases the chances of asthma attacks. It can also increase the risk of heart disease, as irregular breathing and shortness of breath forces the heart to work harder or to even beat irregularly (Delfino et al., 2003). If asthma is not treated properly, patients may also suffer from emphysema, which is associated with a loss of elasticity in the lung tissue (Chang, 2011). Although asthma patients generally experience only momentary attacks of difficult breathing, emphysema patients feel such problems at each individual breathe (Chang, 2011).

7. Conclusion

In terms of both the prevalence and severity, respiratory allergic diseases such as bronchial asthma have drawn a great deal of attention in recent years. In light of their human health significance, we attempted to provide up-to-date information linking these afflictions with air pollution. Evidence has been continuously collected to validate the effect of air pollution upon the development or worsening of allergic respiratory diseases, acting as a co-adjuvant to IgE and/or inflammatory response, in exposed individuals. Asthmatic patients are also at increased risk of developing exacerbations upon exposure to O_3, NO_2, SO_2, PM, dust mites, and mold pollution. However, it is no easy task to evaluate the impact of the individual components of air pollution on the timing of asthma exacerbations and on the prevalence of asthma in general.

As a cautionary measure, efforts to reduce house dust allergens are recommended to prevent or suppress allergies. This knowledge can be integrated into a holistic approach to respiratory health care. Nevertheless, because of the existence of very susceptible populations with the sensitive response capacity, the concept of thresholds for such diseases is not necessarily meaningful in setting standards to regulate allergy-related symptoms or diseases. If one attempts to establish the principle of eliminating adverse effects with an adequate margin of safety, it may not still be practically helpful for the most susceptible groups. Nonetheless, the use of risk reduction strategies will continue to be developed to help support public health. The development of such strategies requires not only qualitative but also quantitative knowledge on the most relevant adverse effects generated from allergy and asthma.

As human response to each allergen is very different from person to person, it is difficult to determine an acceptable (or threshold) level not only for the population as a whole but also those specifically suffering from the diseases. Nonetheless, the quantity of an allergen needed to elicit a response so seriously that a sensitive individual may die should be thousands of times lower than that needed to invoke a sniffle in an equally healthy, but non-sensitized person. Ultimately, therefore, it is recommended to set up a more comprehensive monitoring program in combination with properly designed health studies capable of helping us gain some critical knowledge to elucidate the relationship between ambient air pollution and its health impact in the coming years. A more intensified attempt to bind environmental measurements with questionnaire data on medical symptoms and environmental exposure tests should also be made. Moreover, such effects can be modulated further to derive useful information on environmental risks and to develop protective measures against those diseases. At last, multipronged studies are needed to allow an intimate combination of all available methodologies and to identify both local and general risk factors for asthma and allergies.

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