ABSTRACT

Air quality plays an important role in the increased prevalence of asthma observed in industrialized countries. Recent advances in the study of asthma provide further information on how air pollution affects asthmatics. In this survey of current literature, air pollutants have been loosely categorized according to their location in the environment (occupational, outdoor, indoor). In relation to asthma, these air pollutants have been classified according to their deposition in the lung and their ability to function as an antigen or an irritant. As the study of both air quality and the biology of asthma evolves, classification of air pollutants according to the type of asthma they are most closely related to may provide a method for determining future research goals.
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Introduction

Asthma may be briefly described as a bronchial hyperresponsiveness in which the airways undergo episodes of narrowing resulting in expiratory wheezing. The American Thoracic Society has published guidelines for the diagnosis of asthma (1) which provides a common starting point for studying the disease. Several studies (56,59,70) have suggested a genetic predisposition for asthma, but the pattern of inheritance is far from clear. Asthma can develop in both children and adults and, while episodes can be severe over a short period of time, it can and often does resolve itself without intervention. Severity of the disease can also vary over time and, especially in the case of childhood asthma, may disappear completely later in life. This suggests that although genetic influences are important, the control of asthma is probably exerted on many different levels, some of which may be more open to intervention in the form of prevention or control.

As the study of asthma has evolved, a considerable amount of literature has been produced which examines the relationship between asthma and air quality. While many studies have suggested a connection between airborne pollutants and asthma they have also shown that this relationship is not one of simple cause and effect. Since the prevalence of asthma appears to be on the rise (12,67,72), especially in industrialized countries, resolving this issue will pose a major challenge to regulatory agencies and the research community. Only recently has the pathogenesis of asthma been more clearly defined. Based on this new knowledge, it will now need to be determined which airborne pollutants are likely to cause an increase in the incidence of asthma, and which pollutants are likely to exacerbate the disease in existing asthmatics.

When considering the role of airborne pollutants in the development and course of asthma there are several different processes involved. Some airborne pollutants clearly act as allergens which produce measurable immune responses, while others
appear to act as bronchial irritants by stimulating some undetermined reaction (Figure 1). Research goals must first become oriented to a particular process even though the ultimate aim may be to define more general guidelines for all airborne pollutants. If many pollutants can be defined according to their physical role in the lung, it may become possible to predict future problems based on chemical similarities. Furthermore, as more becomes known about different types of asthma and the degree to which they are related (or unrelated) as a disease process, the ability to predict and prevent potential problems should improve.
Definition of Asthma

Asthma may be divided into categories based on the mechanisms which induce asthmatic episodes and the response to drugs used to control them (bronchodilators and corticosteroids) (60). Extrinsic atopic asthma is mediated through a classic allergic response with an IgE induced hypersensitivity resulting in bronchoconstriction after exposure to airborne allergens. Atopic (allergic) individuals often develop asthma early in life with seasonal responses to a wide variety of allergens, that are generally mediated through IgE. Extrinsic non-atopic asthma is more often brought on by a response to a specific substance. This response may be antibody mediated, although it is not always through IgE. Intrinsic asthma is not induced by any measurable environmental exposure and usually appears late in life. Individuals have no apparent allergies (based on negative skin test) and the asthma becomes persistent rather than episodic, with no seasonal changes and a poor response to bronchodilators.

Occasionally, chronic bronchopulmonary disease may be confused with asthma but this can usually be differentiated by a lack of response to corticosteroids.

Allergic asthma is the most common type of asthma and also perhaps the most well defined. Allergic responses can occur early (10-30 minutes) or late (6-10 hours) after exposure to antigen. On a cellular level (Figure 2) the early allergic response begins with antigen exposure in the airways which results in specific IgE antibody production. The IgE then binds to mast cells causing degranulation and release of early response mediators including histamine, leukotrienes, and, prostaglandins (18). These mediators act directly on smooth muscle receptors and also stimulate autonomic nerve receptors in the bronchial cell wall (23,52) causing contraction of smooth muscle and increased capillary permeability. The late response, which may occur with or without an early response, results from mast cell release of inflammatory cytokines and chemotactic factors which in turn produces an influx of inflammatory cells (macrophages, lymphocytes, and neutrophils) (18). In non-atopic asthma antigen
exposure in the airway may stimulate IgG to function in a similar manner to IgE or the inflammatory cell cascade may be initiated by lymphocytes (54). The early response can also be differentiated from the late response by response patterns to treatment. Early responses are reversed by bronchodilators but are not inhibited by corticosteroids, while late responses are controlled in the opposite way.

The pathological characteristics seen in asthmatics outside of constrictive episodes include increased lung and blood eosinophils, and desquaminated ciliated epithelial cells. During bronchoconstrictive episodes bronchial smooth muscle contracts and mucus secretion increases. These changes diminish airway diameter and impede exhalation (Figure 3). This results in increased resistance to exhaled air, and over time produces a hyperinflation of the lungs which is compensated for by short rapid breaths with the characteristic wheeze upon exhalation. Severe responses resulting in death show edema of bronchial walls, mucus plugs blocking small airways, hypertrophied smooth muscle, excessive sloughing of epithelial cells, and prominent mucus glands upon autopsy (18).

Non specific responses to airway irritants are seen in asthmatics regardless of allergic status. Cold dry air, exercise, and irritating chemicals can induce bronchoconstriction in asthmatics without IgE mediation. Bronchoconstricting drugs such as histamine and methacholine seem to have a much stronger effect in asthmatics and the degree of response seems to correlate with the severity of the asthma (33). This type of response may be related to hyperresponsive autonomic nerves in the bronchial walls and/or a residual effect of the inflammatory process (15). This type of asthmatic reaction in particular needs more definition in order to determine how similar or different it is from a true allergic response.
Measurement of Asthma

Various pulmonary function (PF) tests have been used to measure asthmatic responses on a quantitative basis. The most common testing method used is spirometry which measures expiratory volume. This volume is plotted against rate of exhalation (liters per minute) to determine bronchial resistance. Generally, during an asthmatic attack, expiratory volumes decrease due to increased bronchial resistance. As the lungs residual capacity is filled, the maximum inspiration begins to decrease. Various difficulties are encountered when attempts are made to quantitate these changes. The first problem encountered is the spirometry itself, which is dependant on individual effort and the airway resting tone for maximum inspiration. Since asthmatics have varying degrees of airway resting tone, both among themselves and when compared to non-asthmatics, controversy arises as to which group constitutes the proper control for comparison. The degree of change measured by PF tests also depends on what lung volume the measurement is initiated at. PF tests are generally considered to provide a more sensitive measure of change if measured at partial rather than maximum lung volumes, but the biological relevance of a small change in lung function is not known.

Change in lung function can also be addressed on a qualitative basis by the use of a symptom survey, but since no standard rating scale exists, comparisons between studies are difficult. Retrospective epidemiological studies which rely solely on questionnaires and medical records are very qualitative while some prospective studies may include quantitative testing on some or all of their population. While qualitative measurements may be subject to a high degree of variability, they provide a helpful indication of when bronchial change becomes significant.

Identifying the presence or absence of allergy in asthma is usually based on skin testing for allergic reactions and serologic testing for the presence of specific antibodies. Although these methods do not directly measure the environment in the lung, bronchial lavage (18,54) and bronchial challenge studies (60) of asthmatics
suggest that skin and serologic testing provide a good basis for predicting similar
allergic responses in the lung.
Occupational Air Quality

Occupational air pollution in many ways provides the best possible setting for studying the relationship of specific pollutants to the etiology of asthma. Many airborne chemicals can be easily measured within the workplace and direct comparisons may be made in a controlled chamber exposures. Bronchial provocation with a specific allergen can provide a defined demonstration of effects on airway hypersensitivity. Occupational air pollutants also provide the most direct evidence for actually causing asthma in people with no history of atopy or respiratory disease. Much of the accumulated occupational data is in anecdotal form consisting of individual case reports or casual observances. This has provided direction for more recent work detailing specific responses and latency periods. The most common complication of studying occupational asthma is the "healthy worker effect" which may eliminate asthmatic workers before diagnosis and thus underestimate the degree of the problem. This may be compounded by a medical lack of interest in determining the cause of adult onset asthma, unless the patient specifically implicates work related problems.

With few exceptions occupational asthma develops from a measurable allergic response. Biologically derived products, generally high molecular weight (MW) proteins (summarized in Table 1), have been observed to produce a classic IgE response. The responses most often occur rapidly after exposure and may or may not include a late response. Specific IgE antibodies to fur and urine proteins have been measured in laboratory animal handlers (58,71), and workers in the milling and baking industry to both flour (6) and enzymes used in flour (51). Other enzymes used in the pharmaceutical industry have also been shown produce asthmatic reactions (13,16). Grain and cotton dusts have long been known to produce allergic asthma (17,26), but it is not clear whether this results from the plants or bacterial and fungal contaminants on the plants. Atopy has been shown to be a risk factor for developing allergies to high MW compounds (6,31,57).
Low MW chemicals (summarized in Table 1) such as acid anhydrides (53) and platinum salts (19) have been shown to cause asthma by acting as haptens which require conjugation to some larger molecule (such as human serum albumin) to induce IgE antibodies. Other low MW chemicals such as isocyanates (4) and plicatic acid in western red cedar (74) have not consistently been shown to produce measurable levels of IgE antibody. Low MW chemicals have been shown to produce both early and late reactions but many of the low MW chemicals are particularly consistent producers of late reactions. Atopy does not appear to be a risk factor for developing asthma with low MW compounds (8,14).

This list of compounds is far from complete, but characterizes the variety of initiating processes that ultimately result in the bronchoconstriction of asthma. Site deposition in the lung has not been closely examined for its role in response patterns induced by occupational air pollutants. Particle size and solubility may be a factor in the differences seen between high and low MW compounds. Latency periods for the initial development of occupational asthma can be short (platinum salts-months) or long (isocyanates-years) and extreme sensitivity to particular allergens has been documented. Now that many of these chemicals have been identified according to immunologic activity the potential exists for much needed work to define dose response relationships to both latency and severity. Since atopy may or may not be a predicting factor workers need to be followed closely to relate predisposing factors to the disease progression.
Outdoor Air Quality

When the term air pollution is used, the most common reaction is to think in terms of pollutants which are produced and for the most part remain outdoors. The majority of these are byproducts of the combustion of fossil fuels, which result in the heaviest accumulations in industrial areas or cities with heavy automobile traffic. The pollutants which are most abundant and thus are regulated by the Environmental Protection Agency are nitrogen dioxide (NO₂), sulfur dioxide (SO₂), ozone (O₃), carbon monoxide (CO), lead and particulates. Of these pollutants NO₂, SO₂, and O₃ exert their primary influence in the lung (Table 2). Particulates influence the lung but they are more localized to their emission source and thus have received less attention. Data from both chamber studies and epidemiological studies (25,44,46) suggest that these pollutants act mainly as nonspecific irritants which have not been linked to the development of asthma, but are a problem to existing asthmatics. The exact mechanism of bronchial hyperresponsiveness to nonspecific irritants is unknown, but studies suggest that localization within the lung may be important (38,45,55).

The effect of outdoor air pollution on asthmatics has generally been studied either in carefully controlled chamber exposures or through epidemiological studies of urban and industrial locations. Both methods of study have advantages and disadvantages (summarized in Table 3). Chamber studies have the benefit of carefully controlling exposure conditions and quantitatively measuring responses. These benefits may also hinder the discovery process by missing interactions with other pollutants and limiting the effects of lifestyle, medication, and chronic exposures. Chamber studies can be used to measure two different responses, one being a direct response to a pollutant, and the second being an increased hyperresponsiveness as measured by subsequent bronchial challenge (with bronchoconstricting drugs or cold air). Care must be taken when comparing chamber studies since the criteria used to select the asthmatic population and controls may have a profound effect on the outcome. Outdoor air
epidemiology studies may include quantitative measures such as PF tests but often they rely only on questionnaires and weather and pollution data from stationary points. This means they cannot provide data on individual exposures and can only provide pollutant measurements for a few airborne pollutants. Since industrial pollutants similar to those described as occupational hazards and other natural allergens may also be in the air, their role as confounders is difficult to measure. Questionnaires are used to determine symptoms, lifestyle, medication use and other confounders, but the answers to these questions are very subjective. With epidemiological studies sample size and statistical methods play a crucial role in determining the final conclusions.

Chamber studies which provide acute exposure data on individual pollutants have shown that asthmatics experience bronchoconstriction directly after inhalation of SO₂ (42,68). This response to SO₂ can also be measured in non-asthmatics but to a lesser extent. SO₂ is a water soluble gas which deposits in the upper airways and primarily the nasal cavities when breathing patterns involve partial or total nasal inhalation. Koenig et. al. (45) has demonstrated that the effect of SO₂ is reduced but not eliminated during oronasal breathing when compared to oral breathing alone. SO₂ also reacts with other airborne compounds to form H₂SO₄ which is less soluble and thus deposits lower in the lung. H₂SO₄ has also been shown to produce bronchoconstriction in asthmatics (43,76) although not as consistently as SO₂.

NO₂ which is only partially water soluble is more likely to be deposited lower in the lung. Exposure to NO₂ does not seem to elicit any greater bronchoconstriction in asthmatics at lower concentrations (<1 ppm)(34,50,55) but high concentrations (3-5 ppm) may induce a heightened state of reactivity resulting in a greater response to challenge (50,55). Bauer et. al. (3), by selecting for hyperreactive asthmatics, has been able to show that even low levels (0.3 ppm) of NO₂ can potentiate greater challenge induced bronchoconstriction. O₃, an oxidant which is quite insoluble in water is most likely to reach alveolar portions of the lung and has not been shown to have any greater
effect on asthmatics than non-asthmatics (38,44). Neither NO₂ nor O₃ have been shown to have any greater effect on adolescent asthmatics (46).

A few attempts have been made to combine outdoor air pollutants within the chamber setting by exposing asthmatics to different pollutants sequentially. Rubentstein et. al. (64) has shown that pre-exposure to 0.3 ppm NO₂ did not potentiate any greater response to subsequent exposure to SO₂ in adult asthmatics. On the other hand Koenig et. al. (47) has shown that pre-exposure to O₃ increases hyperresponsiveness to SO₂ in adolescent asthmatics.

Epidemiological studies represent very complex environments. A commonly used approach has been to compare populations in industrialized areas to those in rural areas. Studies based solely on answers to questionaires (30,39), while very non specific, have shown increased levels of air pollution (mainly SO₂ and NO₂) to correlate with an increase in respiratory symptoms. One study in children, which included PF tests (35), showed that increased bronchial reactivity and increased asthma correlated to increased air pollution (again SO₂ and NO₂) without a corresponding change in allergic status. This correlation has not been documented in other similar studies on both children and adults (7,65). Dockery et.al. (25) used baseline PF levels in individual asthmatics as their own controls for PF measurements taken on pollution alert days and demonstrated changes in PF associated with increased air pollution. Reanalysis of this data (10) by different statistical methods attributed the significance of these changes to individual variation and not air pollution. Diary studies may give a better correlation of specific symptoms to actual air levels. Henry et.al. (36) showed no correlation between respiratory symptoms and air pollution levels (SO₂ and NO₂) in asthmatic children. Schwartz (66), who looked at both asthmatics and non-asthmatics, did see a weak relationship between increased SO₂ and recorded chest tightness for asthmatics but Whittemore (81), looking at only asthmatics, found that the pollutant effects were also correlated to temperature and season. Hospital admission data
(2,62,75) have shown a correlation between asthmatic attacks and both temperature and air pollution for both adolescent and adult asthmatics. Hospital admissions data are more likely a measure of severe attacks and thus may represent a select population.

Though chamber studies provide detailed information for individual pollutants, the fact that they control for exposure dose and time, temperature and humidity, and asthmatic severity makes them difficult to compare to epidemiologic studies. While it may never be feasible to do chronic studies in a chamber setting, the importance of combining exposures within a chamber cannot be dismissed since it appears likely that outdoor air pollutants may be interacting with other factors rather than acting as single causative agents. Epidemiological studies cover so many different factors that attempts to pull out a single cause prove difficult as can be judged by the variety of conclusions that have been reached. Some attempts have been made to identify the most important confounders such as temperature and humidity (5,27), ongoing respiratory infection (5), and seasonal allergens (63). These are some of the factors that need to be accounted for in chamber studies along with other potential confounders yet to be discovered. A further complication for both chamber and epidemiological studies is the fact that particle deposition in the lung is affected by the degree of bronchoconstriction present at a given time. The steady state environment in asthmatic lungs and low level chronic allergen and pollutant exposure may prove to play an important roles in the development of responses to non-specific irritants.
Indoor Air Quality

Indoor air pollution is perhaps the newest and the most promising area of research for asthmatics since the general population in industrialized countries spends much more time indoors than outdoors (28). In addition to tobacco smoke, several indoor air pollutants found in homes and office buildings may present a risk to asthmatics or the development of asthma (Table 4). However limited information is currently available. Studies linking social and environmental factors to the development of asthma in children (24,80,83) provide convincing evidence that the home environment of children can affect the potential to develop asthma. The effects of the indoor environment on potentiating bronchial hyperresponsiveness may also be linked to the presence of allergens in the home (11). Since industrial air pollutants have been addressed elsewhere, this section will focus on non-industrial indoor air.

The most common allergens present in the home are dust (including highly allergenic dust mites), fungi, and molds, all of which may be controlled somewhat by adequate ventilation. Dampness in the home, a common result of inadequate ventilation, has been linked to respiratory problems (9) and can increase mold and fungi levels. The most common producers of irritating air pollutants found in the home are tobacco smoke, gas stoves (NO₂), wood stoves (particulates, CO), and kerosene or gas fueled space heaters (NO₂, SO₂, CO). Epidemiological studies linking home environments to respiratory symptoms have correlated the presence of gas stoves (78) with increases in respiratory problems. NO₂ levels in the home can reach levels as high as those shown to enhance bronchial hyperresponsiveness (50,55,73) in chamber studies. Lebowitz et. al. (48) has also shown that interactions between various indoor air pollutants (such as particulates, tobacco smoke, and formaldehyde) can lead to increases in bronchial hyperresponsiveness.

Tobacco smoke, both through direct inhalation or passive smoking, may be one of the most common air pollutants found indoors. The relationship between direct
inhalation and development of asthma (37,77) is weak and it does not appear that the smoking habits of asthmatics differ greatly from the general population which suggest that inhaled smoke is not adversely affecting adult asthmatics. This could be due to the chemical differences between inhaled and sidestream smoke (69), both of which consist of complex mixtures of chemicals and particulates. Passive smoke on the other hand appears to have an significant bronchoconstricting effect on adult asthmatics (20,69). Several studies have also examined the impact of passive smoking on childhood asthma. Maternal smoking has been shown to be related to the development of both recurrent wheezing (32) and new cases of asthma (82,83) in children. A large cross sectional survey by Forastiere et. al. (29) has shown relationships between childhood asthma and both passive smoking and air pollution, but there does not appear to be an additive effect between the two. Other studies have (49,79) not found statistically significant effects of passive smoking on children or adults. It is not yet clear exactly how passive tobacco smoke may function to enhance development of asthma or make the state of hyperresponsiveness worse.

The relationship of indoor air pollution to asthma has only recently become a focus of research and therefore is lacking specific data. One of the difficulties encountered in examining the home environment is similar to the "healthy worker effect" whereby families with allergic or asthmatic members may be more likely to modify the home environment. Passive smoke is especially difficult to study, since it is virtually impossible to find a control group with no exposure. Determination of exact exposure concentrations of passive smoke is also difficult since exposures may be chronic low level or short term high concentration, depending on the distance between the active and passive smoker and the number of active smokers present at a given time.
Conclusions and Future Directions

Major advances have been made in the study of asthma in recent years. The increased level of inflammatory cells and cytokines present in the asthmatic lung (18,41,54) and animal data detailing lymphocyte regulation (via cytokines) of responses to chemical allergens (21,22) provide a basis for the study of all types of asthma. Characterization of the differences between allergic and non allergic asthma may provide further proof of regulation by immune cells in the lung (41,54). Advances in understanding the relationship of inflammation in the lung to bronchial hyperresponsiveness may show that different asthmatic responses are regulated by similar underlying mechanisms. By categorizing the different classes of airborne pollutants with their response patterns, it is possible to link these responses to immune function and gain a better understanding of the entire disease process.

Several issues relating to the link between airborne pollutants and immune function have not yet been addressed. One unanswered question is whether a chemical allergen's molecular characteristics determine immune responses by direct interaction with immune cells or if molecular characteristics determine deposition and fate of molecules such that they do or do not interact with immune cells in the lung. Both direct interaction and solubility characteristics have been implicated, suggesting the possibility of a combined effect. Further study is also needed to determine if the development of asthma is linked to short term high dose exposures or chronic low dose exposures. This is of special interest for occupational asthma since workplace standards are often time weighted, which can allow high concentration exposures over short periods of time. Animal models (40) may ultimately be used to predict threshold levels for occupational allergens. Subpopulations of asthmatics, based on disease severity, need to be identified. This is especially important for epidemiological studies which are so affected by confounding variables.
Airborne pollutants are ever present within the environment. Since the ultimate goal of research is treatment and prevention, the study of asthma must examine events occurring before and after the onset of the disease. By grouping these events in some sequential order, a detailed picture of the entire disease process can be used to achieve these future goals.
Air Pollution

- Occupational
  - allergy $\Rightarrow$ asthma
  - bronchial irritation $\Rightarrow$ (asthma)

- Outdoor
  - bronchial irritation $\Rightarrow$ (asthma)

- Indoor
  - allergy $\Rightarrow$ asthma
  - bronchial irritation $\Rightarrow$ (asthma)

Figure 1. Classification of air pollutants in relation to asthmatic responses.
Figure 2. A simplified representation of cellular interactions in the lung which result in bronchoconstriction.
Figure 3. A cross sectional representation of airways before and during an asthmatic response.
### Table 1. Classification according to molecular weight of some compounds known to cause asthma in occupational settings.

<table>
<thead>
<tr>
<th>High MW</th>
<th>Low MW</th>
</tr>
</thead>
<tbody>
<tr>
<td>animals</td>
<td>diisocyanates</td>
</tr>
<tr>
<td>insects</td>
<td>anhydrides</td>
</tr>
<tr>
<td>grain dust</td>
<td>wood dust</td>
</tr>
<tr>
<td>flour</td>
<td>metals</td>
</tr>
<tr>
<td>enzymes</td>
<td>drugs</td>
</tr>
<tr>
<td>Ambient air pollutants regulated by EPA</td>
<td>Primary Location of health effects</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>------------------------------------</td>
</tr>
<tr>
<td>Nitrogen dioxide</td>
<td>lung</td>
</tr>
<tr>
<td>Sulfur dioxide</td>
<td>lung</td>
</tr>
<tr>
<td>Ozone</td>
<td>lung</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>blood</td>
</tr>
<tr>
<td>Particulates</td>
<td>lung</td>
</tr>
<tr>
<td>Lead</td>
<td>blood</td>
</tr>
</tbody>
</table>

Table 2. Classification of outdoor air pollutants according to location of health effects.
<table>
<thead>
<tr>
<th></th>
<th>advantages</th>
<th>disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chamber</td>
<td>controlled environment</td>
<td>limiting interactions</td>
</tr>
<tr>
<td></td>
<td>single pollutant exposure</td>
<td>limiting lifestyle effects</td>
</tr>
<tr>
<td></td>
<td>select population</td>
<td>select population</td>
</tr>
<tr>
<td></td>
<td>quantitative measurements</td>
<td>acute exposures only</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>encompasses interactions</td>
<td>qualitative measurements</td>
</tr>
<tr>
<td></td>
<td>large sample sizes</td>
<td>inaccurate pollution data</td>
</tr>
<tr>
<td></td>
<td>includes natural allergens</td>
<td>no individual exposure measurement</td>
</tr>
<tr>
<td></td>
<td>measures chronic exposure</td>
<td>dilute population</td>
</tr>
</tbody>
</table>

Table 3. Comparison of methods used to study the effects of air pollutants on asthmatics.
Table 4. Allergens and irritants found indoors which may pose problems for asthmatics.

<table>
<thead>
<tr>
<th>Indoor air pollutants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Home</strong></td>
</tr>
<tr>
<td>dust (dust mites)</td>
</tr>
<tr>
<td>tobacco smoke</td>
</tr>
<tr>
<td>nitrogen dioxide</td>
</tr>
<tr>
<td>molds</td>
</tr>
<tr>
<td><strong>Work</strong></td>
</tr>
<tr>
<td>tobacco smoke</td>
</tr>
<tr>
<td>dust</td>
</tr>
<tr>
<td>molds</td>
</tr>
<tr>
<td>volatile organic compounds</td>
</tr>
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