## **Asthma Research and Resources**

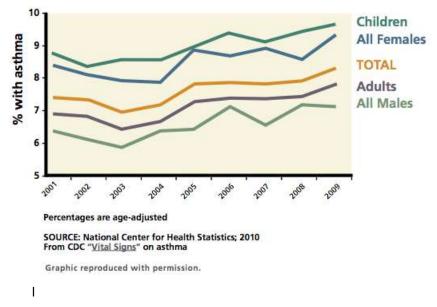
By Jessica Hale, Student Intern Summer 2016

## What is Asthma?

Asthma is a serious and widespread chronic disorder of the bronchial tubes in the lungs (the "airways"). Typically, people with asthma experience recurrent attacks of breathlessness and wheezing, however, chest tightness or coughing can also occur. The underlying process includes chronic inflammation of the airways, reversible obstruction of the flow of air in and out of the airways, and the tendency of the airways to over-react to stimuli. Asthma most commonly develops in early childhood, and more than three-quarters of children who develop asthma symptoms before age 7 no longer have symptoms by age 16. However, asthma can develop at any stage in life, including adulthood. As reported by the American Lung Association, asthma is one of the most common chronic disorders in childhood and a leading cause of hospitalization in children. It is also one of the leading causes of school absenteeism.

## **Current Condition**

According to the CDC, the rates of asthma are increasing.<sup>3</sup> In 2014, asthma affected 7.7% of the U.S. population, equivalent to 24,009,000 people. The rates were higher among children at (8.6%) than in adults (7.4%). Females (9%) in the U.S. experience asthma at greater rates than males (6.3%).<sup>4</sup>



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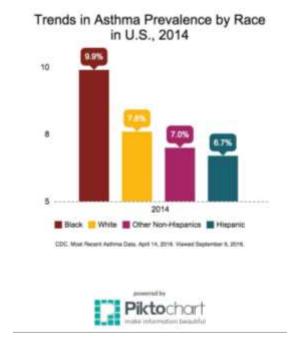
Ethnic groups are also burdened with asthma at different rates. Recent data is available for four ethnic groups depicted in the chart to the right. Data from 2008-2010 reports asthma prevalence for more ethnic groups:<sup>5</sup>

Persons on multiple races: 14.1

American Indian or Alaska Native: 9.4

Asian: 5.2

Globally, it is estimated that 235 million people suffer from asthma. Most asthma-related deaths occur in low- to lower-middle income countries. Overall, asthma is underdiagnosed and undertreated, leading to substantial burden and a lower quality of life.<sup>6</sup>



## **Causes**

People with asthma present similar symptoms, however, the origins, triggers, and underlying pathology of the disease differs considerably. Asthma is a multifactorial disease, meaning there are many factors responsible for its onset. The factors playing a predominant role in asthma development will differ with each case. While the causes of asthma are not completely understood, it is generally accepted that asthma is caused by a combination of genetic predisposition and environmental contributors. Environmental contributors are typically inhaled substances that irritate airways. There is greater research on asthma triggers (factors that cause asthma attacks or make it worse) than on asthma causes.

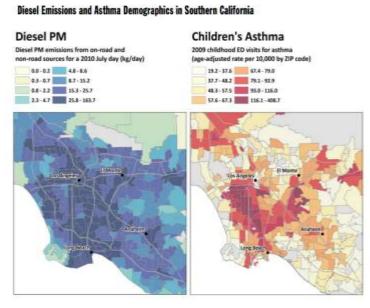
### **Environmental Contributors**

There is no scientific consensus on what environmental factors could be involved but recent research suggests a few possibilities.

#### Climate Change and Outdoor Air Pollutants:

 The changing climate has the potential to increase production of ozone and fine particulate matter. This can trigger inflammation of the lungs and reduced lung function as well as chest pain and coughing.<sup>10</sup>

- Kids who frequently engage in sports activity in areas of high ozone are at greater risk of developing asthma.<sup>11</sup>
- Increasing carbon dioxide concentrations affect the timing of allergen distribution, amplifying the allergenicity of pollen and mold spores.<sup>12</sup>
- Unchecked global warming will worsen allergies due to longer growing seasons for allergens. More airborne allergens could lead more asthma attacks for 10 million Americans with allergic asthma.<sup>13</sup>
- Increasing precipitation due to climate change can increase mold spores.<sup>14</sup>
- Increasing frequency of droughts can increase dust and particulate matter.
- Increasing wildfire activity due to global temperature changes has the potential to exacerbate asthma and increase asthma ED and hospital visits.<sup>16</sup>
- Short-term exposures to ozone, nitrogen dioxide, sulphur dioxide, particulate matter (2.5), and TRAP (complex mixture of particulate matter derived from combustion, non-combustion, and primary gaseous sources) is thought to increase the risk of exacerbated asthma symptoms.<sup>17</sup>
- Increasing amounts of evidence also suggest that long-term exposures to air pollution, especially TRAP and its surrogate, nitrogen dioxide, can contribute to new-onset asthma in both children and adults.<sup>18</sup>
- Previous evidence suggests that children exposed to wood or fossil fuel smoke, soot, or exhaust (1), herbicides (2), pesticides (3), and farm crops, farm dust, or farm animals (4) are 1.74 times, 4.58 times, 2.39 times, and 1.88 times more likely to be diagnosed with asthma by age five.<sup>19</sup>
- Several lines of evidence suggest that components of diesel exhaust may cause asthma.<sup>20</sup> This is supported by studies finding that children growing up along streets with heavy truck traffic are more likely to develop asthma-related respiratory symptoms.<sup>21, 22</sup> Health. ATSDR,



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## Indoor Air Pollutants:

- Previous evidence also suggests that cockroach exposure is associated with a 2.03 times increased risk for diagnosis of asthma by 5 years of age.<sup>23</sup>
- Combustion of biomass fuels continues to be the main source of household energy for 2.4 billion people worldwide. There is concern for respiratory irritation from the particulate matter and gases released from using simple cook-stoves within homes that lack adequate outdoor ventilation. Research is suggestive that biomass smoke exposure is associated with asthma. However, more research is needed to establish a relationship of similar strength as biomass smoke and chronic bronchitis in adults and acute lower respiratory tract infections in children.<sup>24</sup>

### Causes of Asthma:

- Diesel exhaust (PM2.5 and Nitrogen dioxide)
- Ozone

### Associated with Asthma:

 Prenatal and postnatal exposure to secondhand tobacco smoke

## Exacerbation of Asthma:<sup>25</sup>

Many exposures are known to exacerbate asthma. Information in the first table below comes from following source unless otherwise indicated: Kanchongkittiphon W et al. Indoor environmental exposures and exacerbation of asthma: An update to the 2000 review by the institute of medicine. Environmental Health Perspectives. January 2015; 123(1): 6–20. The "strong" (Red), "good" (orange), and "limited" (yellow) categories are taken from the CHE Toxic and Disease Database structure.

Substance	Notes
Acids <sup>26</sup>	
Air pollution <sup>27</sup>	
Ammonia <sup>28</sup>	
Cat allergen	Individuals must be sensitized to cats
Chlorine <sup>29</sup>	
Cockroach allergen	Individual must be sensitized to cockroaches
Cotton dust <sup>30</sup>	

Dampness or dampness-related agents (like mold)	In children
Strong evidence	
Diesel exhaust <sup>31</sup>	
Environmental tobacco smoke (ETS)	In preschool-age children
House dust mite allergens	Individual must be sensitized to dust mites
Nitrogen dioxide <sup>32</sup>	
Outdoor culturable fungal exposure	Individual must be sensitized to fungi
Oxone <sup>33</sup>	
Sulfur dioxide <sup>34</sup>	
Tobacco Smoke <sup>35</sup>	
Rodent allergens	Only causally tested in lab settings and individual must be sensitized to rodents
Endotoxins	
Organophosphates <sup>36</sup>	
Pesticides <sup>37</sup>	
Dampness or dampness-related agents (like mold)	In adults
Dog allergens	Individuals must be sensitized to dogs
Painting or renovation <sup>38</sup>	
Phthalate plasticizers <sup>39</sup>	
Some aromatics	
Formaldehyde	
Domestic birds	Individual must be sensitized to birds
Exposure to certain fragrances	Individual must be sensitized to the exposure

## Hygiene Hypothesis

- Some hypothesize that kids are growing up "too clean". Under this interpretation, in normal childhood development kids are routinely exposed to a range of childhood diseases, domestic animals, and bacteria. When kids are protected against these challenges because of better health care and better personal hygiene, their immune systems become over-reactive, or hyper-sensitized, to asthma allergens.
- While this hypothesis has received attention in the press, it is not consistently supported
  by the scientific evidence. It fails to explain the higher risk faced by African-American
  children and by urban children compared to suburban children, as well as the increases
  in asthma seen in developing countries like China and India. Overall, the risk for
  developing asthma is not as simple as germ exposure.<sup>41</sup>

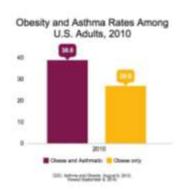
Interactions among these different exposures may be important in the development of asthma. For example, an older study found that asthma symptoms in children ill with a respiratory virus are likely to be more severe if they are exposed to the air pollutant nitrogen dioxide, even at levels of nitrogen dioxide below current air quality standards. <sup>42</sup> In another study, combining exposure to low levels of pollen with exposure to levels of pollutants commonly found in urban air dramatically worsened asthma symptoms. <sup>43</sup>

In addition, infections (such as respiratory syncytial virus (RSV))<sup>44,45</sup>, some drugs (such as acetaminophen<sup>46</sup>), and sulfites (food additives used in dried fruit, wine, dehydrated potato products, shrimp, etc.)<sup>47</sup> may be associated with asthma risks.

# **Lifestyle Factors**

#### Obesity:

- Obesity increases the risk of developing asthma, worsens asthma symptoms, and leads to poor asthma control. 48,49
- According to a study done by the CDC in 2010, more people are obese and asthmatic than obese and nonasthmatic.<sup>50</sup>
- Almost every state reported higher rates of people with asthma who are obese.<sup>51</sup>





## Smoking:

- Cigarette smoking is one of the most common asthma triggers. The gases and particles from both first- and second-hand smoke can severely irritate the airway of all individuals, especially those with asthma.<sup>52</sup>
- Nonetheless, 21% of people with asthma smoke. This rate is greater than the 17% of people without asthma who smoke.<sup>53</sup>

#### Stress:

- Social stressors, such as violence, can increase the risk of asthma. Stress can add to and even magnify the impacts of exposure to other environmental conditions that foster the onset or increase the severity of asthma.<sup>54</sup>
- The mechanism believed to be responsible is the theory of allostatic load, in which chronic stress causes wear and tear on the body and its mechanisms.<sup>55</sup> Learn more about allostatic load on CHE's Psychosocial page.
- One study found that if there was intimate partner violence in the home, the child (ages 0-3 years of age) had double the risk of developing asthma. This risk increased if the mother had limited interactions with the child and decreased with greater interaction.<sup>56</sup>
- The multifactorial quality of asthma was identified in a study that showed the risk of new onset asthma attributable to traffic related air pollution (TRP) being significantly higher for children whose parents were subject to higher amounts of stress.<sup>57</sup>

#### Low socioeconomic status:

• Families reporting a lower socioeconomic status are more likely to attend a school with heavy traffic roads nearby. 58 As mentioned earlier, closer proximity to high traffic areas put individuals at greater risk for asthma development.

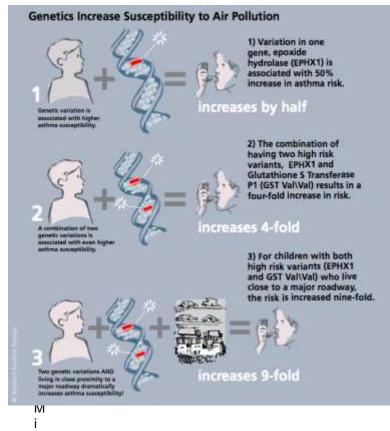
# **Occupational Exposures**

Within the U.S. in 2012, an estimated 1.9 million cases of asthma among adults were work-related, accounting for 15.7% of current adult asthma cases.<sup>59</sup> The occupations reporting the highest rates of asthma are paint sprayers, bakers and pastry makers, nurses, chemical workers, animal handlers, welders, food processing workers, hairdressers and timber workers.<sup>60</sup> Occupational exposures linked to asthma attacks include these:<sup>61</sup>

- Wood dust
- Flour and grain dust
- Colophony (an ingredient in printing inks, varnishes, glues, and sealing wax)
- Isocyanate chemicals (used in foams, plastics, paints, and varnishes)
- Soldering fluxes
- Latex
- Aldehydes

## **Genetic Susceptibility**

In addition to environmental factors, an individual's genes can make them more or less at risk of developing asthma. Having a family history of asthma does increase an individual's asthma risk, however, inheritance does not follow a straightforward pattern.<sup>62</sup> Many genetic factors are shown to increase asthma susceptibility, especially when exposed to major roads<sup>63</sup> and certain allergens.<sup>64</sup> The genes glutathione (GST) and epoxide hydrolase (EPHX1) are important for detoxification and elimination of contributors to oxidative stress associated with asthma. Certain genetic variants in GST and EPHX1 are individually associated with increased risk of developing asthma.65 Since asthma is a multifactorial condition, one study found a nine-fold increase risk for lifetime asthma among those in the high risk group of GST, EPHX1, and proximity to a major roadway.66



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Due to allergies being a major component of asthma exacerbation, there is significant genetic component for asthma caused atopy. Atopy refers to the genetic tendency to develop allergic diseases, such as asthma, rhinitis, and eczema. It often leads to heightened immune responses to common allergens.<sup>67</sup>

# Window of Vulnerability: Early Life Exposures

Environmental exposures early in life (before birth and during infancy) can be important in setting the stage for later development of asthma.

#### Harmful Contributors:

 Certain chemicals alter lung structure and function during development. These include pesticides, dioxin, nicotine, naphthalene, ozone, arsenic, and phthalates.<sup>68</sup>

- One study found that pregnant mothers exposed to both polycyclic aromatic hydrocarbons (PAHs - released from burning substances), air pollutants from gasoline and other fossil fuels, and secondhand tobacco smoke were more likely to have children with asthma.<sup>69</sup>
- Early life exposure to allergens (house dust mites, furred pets, cockroach, rodent and mold), air pollution (nitrogen dioxide, ozone, volatile organic compounds, and particulate matter), and viral respiratory tract infections (respiratory syncytial virus and human rhinovirus) is implicated in the development of asthma in high risk children.<sup>70</sup>
- Studies are focusing on immune system development and immune system cells, especially the two types of T-helper cells. If a baby has too high a proportion of one of these types, they are much more likely to develop asthma symptoms.<sup>71</sup>
- Maternal obesity during pregnancy is associated with increased risk of asthma in offspring.<sup>72</sup>
- Recent studies suggest prenatal BPA exposure is associated with childhood wheeze/asthma, although the data is limited<sup>73</sup>

### Protective Contributors:

- Exposure to microbial diversity in the perinatal period may diminish the development of atopy and asthma symptoms.<sup>74</sup>
- Breastfed infants are less likely to develop asthma and allergies compared to those fed infant formula.<sup>75</sup> Breast-feeding enhances immune function.
- Higher vitamin D intake during pregnancy is associated with decreased risk of wheeze in early childhood. Reduced risk of wheezing may be due to reduced frequency of respiratory infections.<sup>76</sup>
- Microbiome: A healthy gut is full of good bacteria and other microbes that promote a working immune system's ability to fight off bad bacteria and other pathogens. Broad exposure to a wealth of non-pathogenic microorganisms early in life are associated with protection against many health conditions. Studies found that first-year infants exposed to house dust, high in levels of mouse, cockroach, or cat allergens, and a variety of bacteria report significantly lower rates of allergies and recurrent wheeze at age three.<sup>77</sup> For more information, visit CHE's Microbiome Research and Resources page.

# **Economic Costs**

Globally, the economic costs associated with asthma are estimated to exceed the costs of HIV/AIDS and tuberculosis combined. 78 According to the CDC, the monetary costs of asthma in 2007 was \$56 billion for the U.S. This estimate combines medical costs, lost school and work days, and early deaths. There was a 6% increase from the cost of asthma in 2002, which was \$53 billion. Not only is asthma costing the nation, but the medical costs are burdensome for the individual. About 2 in 5 (40%) uninsured people with asthma could not afford their prescription medicines and about 1 in 9 (11%) insured people with asthma could not afford their prescription medicines. 79 Another study estimated that the costs of childhood asthma attributed solely to air pollution within just two cities of California is \$18 million each year.80

## What We Can Do

Targeted primary prevention for asthma-related risk factors is limited since we have not definitively identified what promotes asthma development. Better understanding of the causes of asthma is urgently needed, but in the interim we should focus on improving lung and overall health. This includes reducing exposure to tobacco smoke, reducing indoor and outdoor air pollution, reducing occupational exposures, reducing childhood obesity, improving maternal health, and encouraging breastfeeding.<sup>81</sup> As a collective, we can reduce our exposures to environmental triggers. Decreasing vehicle use and utilizing alternative transportation options, such as walking and biking, will promote healthier lifestyles as well as benefit our environment. However, with greater outdoor activity there is a potential increase of exposure to harmful outdoor air pollutants in urban areas. 82 If possible, walking and biking routes, homes, and schools should be away from major roadways with heavy traffic.83

This document is student work. CHE makes no claim that all the information has been verified.

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