

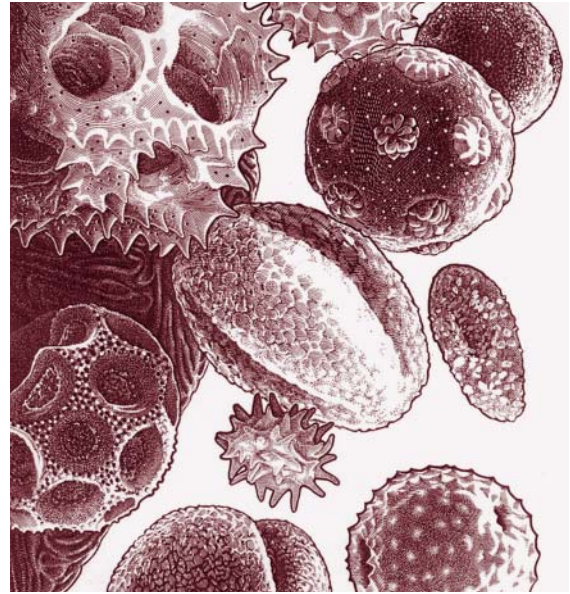
## ASTHMA AND ALLERGIC DISEASES

Asthma and allergic diseases are among the major causes of illness and disability in the United States. Chronic allergic conditions can significantly decrease quality of life, patient well-being, employee productivity, and school performance and attendance. Estimated annual healthcare costs are more than \$14 billion. NIAID's goal in asthma and allergic diseases research is the development of more effective treatments, prevention strategies, and behavioral interventions.

Approximately 50 percent of Americans have positive skin tests to at least 1 of 10 allergens known to contribute to allergic illness.<sup>14</sup> These allergens include ragweed, Bermuda grass, rye grass, white oak, Russian thistle, *Alternaria* (a mold), cat, house dust mite, German cockroach, and peanut. The prevalence of allergic rhinitis (hay fever) varies widely among different countries, from 2 to 40 percent.<sup>15</sup> The prevalence of allergic rhinitis has increased substantially over the past 15 years<sup>16</sup> and is estimated to be 9.9 to 16 percent in the United States.<sup>17,18</sup>

Atopic dermatitis is one of the most common skin diseases worldwide, particularly in infants and children. The estimated prevalence of atopic dermatitis in the United States ranges from 9 to 30 percent<sup>19,20</sup> and appears to be increasing.<sup>21,22</sup>

Food allergy occurs in 6 to 8 percent of children aged 6 years or younger and in 2 percent of adults.<sup>23</sup> The prevalence of allergy to cow's milk in young children is 1.9 to 3.2 percent and to egg is 2.6 percent.<sup>24</sup> Other food allergens affect children and adults, including allergy to peanuts and tree nuts, which is estimated at 1 percent of the



*Pollen grains that can trigger allergies  
(Colorized electron micrograph magnification)*

U.S. population.<sup>25</sup> These two foods are the leading causes of fatal and near-fatal food allergic reactions. About 30,000 Americans per year have anaphylaxis to food, and about 150 Americans, usually adolescents and young adults, die annually from food-induced anaphylaxis.<sup>23,26</sup> Food allergy is the most frequent single cause of emergency room visits for anaphylaxis and accounts for 34 to 52 percent of such emergency room visits.<sup>27,28</sup>

In 2001, 73 people per 1,000 or 20.3 million people had current asthma diagnosed by a health professional (current asthma prevalence), and 43 people per 1,000 or 12 million people had experienced an asthma attack in the previous year (asthma attack prevalence). Asthma disproportionately affects children and minority populations, particularly non-Hispanic blacks. The current asthma prevalence among children aged 0 to 17 years was 87 per 1,000 or approximately 6.3 million children, and the asthma attack prevalence was 57 per 1,000 or 4.2 million children.

Current asthma prevalence was about 10 percent higher among non-Hispanic blacks compared with non-Hispanic whites and about 40 percent higher compared with Hispanics. Non-Hispanic blacks had an asthma attack prevalence about 20 percent higher than non-Hispanic whites and almost 60 percent higher than Hispanics. This disparity was greater among children: asthma was more prevalent among black children aged 17 years and younger than among white children of the same age.<sup>29</sup>

In 2000, asthma was the first-listed diagnosis for 465,000 hospitalizations, and 214,000 of these were recorded for children aged 18 years and younger. Hospitalization rates were highest among children aged 0 to 4 years, with a rate of 67 people per 10,000. The asthma hospitalization rate for blacks was 220 percent higher than for whites, and females had a 25 percent higher hospitalization rate than males. Asthma accounted for 10.4 million outpatient visits and 1.8 million emergency department (ED) visits in 2000. Children aged 0 to 17 years had more than 728,000 ED visits due to asthma, a rate of 104 people per 10,000, and the ED visit rate was highest among children aged 0 to 4 years at 180 people per 10,000. Adults 18 years and older had 54 ED visits due to asthma per 10,000. The ED visit rate due to asthma for blacks was 125 percent higher than that for whites, and for females about 30 percent higher than that for males.<sup>29</sup>

In 2000, 4,487 people died from asthma, or 1.6 per 100,000. Non-Hispanic blacks were the most likely to die from asthma and had an asthma death rate over 200 percent higher than non-Hispanic whites and 160 percent higher than Hispanics. Females had an asthma death rate about 40 percent higher than

males.<sup>30</sup> The economic costs of asthma continue to rise. In 1998, asthma accounted for an estimated \$12.7 billion in expenditures, with \$7.4 billion in direct medical expenditures and \$5.3 billion in indirect costs.<sup>31</sup>

The cause, pathogenesis, diagnosis, treatment, and prevention of asthma and allergic diseases represent major areas of emphasis for NIAID's Division of Allergy, Immunology, and Transplantation (DAIT). NIAID vigorously pursues research on asthma and allergic diseases by fostering investigator-initiated projects and by supporting cooperative clinical studies, a national network of research centers, and demonstration and education research projects.

The Inner-City Asthma Study (1996–2001), co-funded by NIAID and the National Institute of Environmental and Health Sciences (NIEHS), was a multicenter randomized controlled trial that tested the effectiveness of two interventions in reducing asthma morbidity among inner-city children with moderate to severe asthma. The two interventions were (1) a physician feedback intervention that provided physicians with up-to-date information on participants' recent asthma symptoms, medication use, and healthcare utilization; and (2) an environmental intervention aimed at reducing exposure to environmental triggers, including environmental tobacco smoke, cockroaches, house dust mites, mold, furry pets, and rodents. A total of 941 patients were recruited and evaluated for a 1-year intervention and for an additional year of follow-up after the intervention was completed. The physician feedback intervention reduced unscheduled clinic or ED visits but had no significant

effect on asthma symptoms. The environmental intervention significantly reduced asthma morbidity during both the treatment and the follow-up year, and the magnitude of reduction correlated with the reduction in cockroach and house dust mite allergen levels in dust collected from the children's bedroom floors.

A substudy of the Inner-City Asthma Study, jointly funded by NIAID, NIEHS, and the U.S. Environmental Protection Agency (EPA), evaluated the impact of indoor and outdoor fine particles and co-pollutants on respiratory morbidity. Data from this study demonstrate that outdoor particles contribute approximately 25 percent to the indoor particle concentration, that smoking is the major source of indoor particles, and that indoor concentrations of fine particles peak in the late evening in homes where smoking occurred, perhaps reflecting the influence of after-dinner smoking. Analysis of data pertaining to the effects of particle concentrations on asthma symptoms is currently under way.

In 2001, NIAID collaborated with the Centers for Disease Control and Prevention to launch a program to disseminate and implement the very successful asthma intervention developed by the NIAID National Cooperative Inner-City Asthma Study (NCICAS, 1991–1996). This educational and behavioral intervention, delivered by an asthma counselor, has been shown to reduce symptoms and hospitalizations in inner-city children with moderate to severe asthma. NIAID-funded investigators translated the NCICAS research intervention into a form that can be efficiently used in a variety of healthcare delivery settings, including health maintenance organizations, health departments, and

community clinics. The 4-year program targets children living in inner cities and is being implemented through 23 inner-city healthcare organizations throughout the United States. More than 6,000 inner-city children with asthma will benefit from the effort.

In 2002, NIAID established the Inner-City Asthma Consortium (ICAC) to evaluate the safety and efficacy of promising immune-based therapies to reduce asthma severity and prevent disease onset in inner-city children. ICAC also will conduct research to determine the mechanisms of action of the immune-based therapies; develop and validate biomarkers to measure disease stage, progression, and therapeutic effect; and understand the immunopathogenesis of asthma in inner-city children.

The NIAID Asthma and Allergic Diseases Research Centers program is the cornerstone of the pathobiology component of the Institute's asthma and allergy research program, providing support for basic and clinical research on the mechanisms, diagnosis, treatment, and prevention of these diseases. In response to the recommendations of an expert panel convened in February 2000, the program requirements were revised to emphasize studies in humans. NIAID currently supports a national network of 13 Asthma and Allergic Diseases Research Centers, two of which are co-funded by NIEHS.

The Immune Tolerance Network (ITN), co-sponsored by NIAID, the National Institute of Diabetes and Digestive and Kidney Diseases, and the Juvenile Diabetes Research Foundation International, is an international consortium of basic scientists and clinical

investigators that performs clinical trials and mechanistic studies designed to evaluate the safety and efficacy of promising approaches to tolerance induction for the treatment of immune-mediated disorders, including allergy and asthma. It has completed one trial of DNA-ragweed allergen conjugates for the treatment of allergic rhinitis. Preliminary data suggest that this conjugate, when given to ragweed allergic patients prior to the 2001 ragweed season, reduced symptoms in both the 2001 and the 2002 ragweed seasons. The ITN currently is conducting a trial to determine the efficacy of the combination of anti-IgE (omalizumab) and ragweed allergen immunotherapy for treatment of allergic rhinitis. More information on the ITN is available on its Web site at [www.immunetolerance.org](http://www.immunetolerance.org).

An important NIAID intramural study is examining how allergen immunotherapy (AIT) works to reduce or prevent reactions to allergens such as pollen, dust, or cat dander. Although the efficacy of AIT in asthma is modest, it remains the only known disease-modifying therapy for allergic asthma. Certain types of white blood cells, called Th2 cells, produce substances that generate allergies,

whereas others, called Th1 cells, produce substances that may inhibit the development of allergies. This study will determine whether AIT changes the immune response to allergens by reducing the number of Th2 cells or by converting them into Th1 cells. A better understanding of the mechanisms underlying the clinical effectiveness of AIT might help scientists to discover new approaches to treating allergies and asthma.

Scientific advances over the past several decades have revolutionized our understanding of the human immune system and have contributed significantly to extraordinary improvements in the treatment of many immune-mediated diseases. As the primary NIH Institute for research in immunology, NIAID has been at the forefront of many of these advances, including discoveries leading to the characterization of asthma and allergic diseases as immunologic disorders. With an enhanced understanding of the role of immune dysfunction in the pathogenesis of asthma and allergic diseases, NIAID is uniquely positioned to apply fundamental knowledge to develop novel therapies and eventually to prevent disease onset.