Advances in adult and pediatric asthma

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This review summarizes the highlights in the study of adult and pediatric asthma from October 2002 through October 2003. It is easiest to categorize this year's advances into physiologic, epidemiologic, therapeutic, and primarily pediatric developments. In physiology the identification of the *ADAM33* gene as an asthma susceptibility gene has led to a new hypothesis concerning the pathogenesis of asthma. Understanding the integration of the upper and lower airways is likely to have important implications for patient management. Epidemiologic studies continue to show that asthma is a significant and costly disease, with medications comprising the most significant direct costs. Early intervention and improved management can significantly reduce the burden of illness. Research presented indicates there is an opportunity for allergist-immunologists to improve diagnostic and therapeutic approaches to asthma management. Our community has a strong commitment to health care quality, education, and delivery. The *Journal* will reflect this commitment with a new section devoted to these issues. (J Allergy Clin Immunol 2004;113:407-14.)

Key words: *Asthma, adult asthma, pediatric asthma, adherence, disease management, epidemiology, drug therapy, medical economics, atopy, minorities, inhaled corticosteroids, health disparities, guidelines, allergic bronchopulmonary aspergillosis, omalizumab, montelukast, clinical research*

As in our previous review of advances in clinical asthma in the *Journal of Allergy and Clinical Immunology* (JACI),[1,2] there are further advances in physiology, epidemiology, and therapeutics that have been made in 2002 and 2003, and these are summarized in Tables I and II. Although our goal is to review for our readership highlights published in the JACI over the past year, we have included a few references from other journals particularly relevant to this focus. The continued interest of our readers in health care quality, education, and delivery has led to a new American Academy of Allergy, Asthma and Immunology Interest Section of Health Care Delivery and Quality. In the JACI we introduce a section devoted to health care issues.

Abbreviations used
BHR: Bronchial hyperresponsiveness
eNO: Exhaled nitric oxide
FP: Fluticasone proprionate
H_2O_2: Hydrogen peroxide
ICS: Inhaled corticosteroid
JACI: *Journal of Allergy and Clinical Immunology*
SNP: Single nucleotide polymorphism

THE PHYSIOLOGY OF ASTHMA

Becoming gene-iuses

Elucidating genetic mechanisms will improve our understanding of the pathogenesis of asthma and the interaction of genes with the environment and lead to new diagnostic and preventative approaches.[3] Important chromosomal linkage regions and several candidate genes have been previously identified. Van Eerdewegh et al[4] identified a gene associated with asthma and bronchial hyperresponsiveness (BHR). This gene, *ADAM33*, located on the short arm of chromosome 20 (20p13), yields a protein that is a metalloprotease and a disintegrin and that has a variety of other functions.[5,6] The ADAM33 protein is found in airway fibroblasts and smooth muscle but not in T lymphocytes and inflammatory cells associated with asthma. This raises the possibility that the inciting event in the development of asthma is not inflammation alone. Primary abnormalities in the fibroblast and smooth muscle cell function might play an important role and might participate in an additional, possibly synergistic, pathophysiologic pathway.[6]

Howard et al[7] examined the occurrence of single nucleotide polymorphisms (SNPs) in *ADAM33* associated with asthma in American ethnic groups. No single SNP was found to be associated with asthma in all 4 groups (African American, US white, US Hispanic, Dutch white), but at least one SNP was associated with asthma in each group. The investigators concluded that their replication of the original *ADAM33* findings in different populations strengthens the hypothesis that this gene is important in the development and pathogenesis of

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TABLE I. Key advances in adult asthma reported from October 2002 through October 2003

The new ability to map the human genome makes it possible to study gene-environment interactions.
As new immune-mediating pharmaceuticals enter the marketplace, postmarketing drug surveillance becomes even more important.
Lung imaging innovations might allow better definition of airway collapse in asthma.
The patient-physician interaction is extremely important for understanding patients' barriers to adherence, which might include inability to meet copayments, concern about risks of chronic medications, and trust of the medical establishment.
Longitudinal studies of the relationship of ICSs and bone loss continue to be important.
Antifungal therapy shows promise as adjunctive therapy in ABPA.

ABPA, Allergic bronchopulmonary aspergillosis.

TABLE II. Key advances in pediatric asthma*

Origins and natural history of asthma
Risks factors for persistence of asthma and relapse after remission include house dust mite sensitization, airway hyperresponsiveness, female sex, smoking, and early age of onset.
Additional sources of allergen and endotoxin exposure include daycare centers and schools.
There is a complex relationship among environment, allergen sensitivity, infection, and time of exposure in the development of asthma.
Management of asthma in children
An evidence-based guidelines approach and increased use of controller medication can effectively stabilize urgent-care visits because of asthma.
Significant airway remodeling can be present despite normal pulmonary function and high-dose corticosteroid therapy in patients with difficult to control asthma.
New measures are available to assess asthma control in children, including eNO and impulse oscillometry.

*Based on literature available between October 2002 and October 2003.

asthma. Recently, Lind et al[7a] failed to find an association between ADAM33 and asthma in Puerto Rican and Mexican populations. We can expect more studies examining this gene and associated hypotheses of airway remodeling in asthma.

The accuracy of the identification of relevant genes is only as good as the characterization of the phenotype and the clinical definition of disease.[3,8] For example, the phenotype used for the study by Van Eerdewegh et al[4] was "physician's current diagnosis of asthma and active asthma medication use." They performed a second analysis restricting the definition by adding an additional requirement of BHR and increased the statistical significance of the result by a factor of 10. The significance was not improved when they included increased serum IgE levels, supporting the theory that atopy and BHR might have different mediators. Thus to understand which polymorphisms are critical for an asthma phenotype, it is essential to begin with valid clinical definitions of asthma and also allergic rhinitis. Clinical epidemiology will play a growing role in these investigations, which link clinical, basic science, and genetic studies.

The integration of the respiratory system

Allergic asthma and allergic rhinitis are believed to be linked or "integrated."[9,10] Togias[10] states that successful management of chronic allergic respiratory syndromes requires an understanding of the interactions of the upper and lower airways. Kelly et al,[11] using a new segmental bronchoprovocation technique for allergen challenge, instilled saline or ragweed into a bronchus and collected bronchoalveolar lavage fluid. The bronchoalveolar lavage fluid of all 18 ragweed-sensitive patients, 9 with asthma and 9 with allergic rhinitis without asthma, had similar patterns of cellular recruitment, mediators, and cytosine generation, but the dose of allergen required for a response was significantly less in the patients with asthma. These data suggested that the inflammatory response was the same but that patients with asthma might have increased airway sensitivity as a result of preexisting injury or airway remodeling.

Sandrini et al,[12] in a double-blind, parallel-arm, placebo-controlled trial, randomized 23 adults with allergic rhinitis, 16 of whom had asthma, to topical nasal steroid or placebo for 4 weeks. Exhaled nitric oxide (eNO) and hydrogen peroxide (H_2O_2) levels in exhaled breath condensate were measured. Although eNO and H_2O_2 levels decreased in treated patients, there were no significant changes in BHR, nasal and asthma symptoms, or peak flow rates with treatment. Because eNO levels decreased significantly after treatment with topical nasal steroid only in the subgroup of patients with asthma but H_2O_2 decreased in all subjects, the investigators concluded that eNO might be a more specific marker of lower airway inflammation. Determining noninvasive markers of asthma exacerbation has important implications both for research and clinical care.

Imaging the lungs

Imaging the ventilated air spaces of the lung has challenged researchers. Samee et al,[13] using hyperpolarized helium 3 with magnetic resonance imaging, reported a correlation between the number of ventilation defects among patients and percent predicted FEV_1. They also demonstrated an increased number of defects in ventilation after exercise and methacholine challenges. Such imaging is likely to improve our understanding of the pathophysiology of asthma.

EPIDEMIOLOGY

Worldwide

Asthma is a cause of morbidity worldwide.[14-16] Encouraging information was provided by Stafford et al,[16] who reported an increase in controller-to-reliever prescriptions in the United States, which is consistent with evidence-based guidelines. They also noted a concomitant leveling off of an earlier trend for an increase in asthma visits.[14-16] Unfortunately, controller medications are costly. Lai et al[15] surveyed 8 urban areas in the Asia-Pacific region and found underuse of inhaled corticosteroids (ICSs). Not specifically addressed by this article is the unavailability of these efficacious medications for many patients because of their cost.

At home

Improving self-management and adherence to ICSs remains a challenge. Apter et al[17] evaluated potentially modifiable predictors of ICS adherence at the patient-physician interface in a cohort study of mostly urban African American subjects with moderate or severe persistent asthma. Patients' beliefs in the risks compared with benefits of ICSs were associated with lower adherence. Subsequently, they conducted focus groups of 15 urban African American asthmatic adults, exploring beliefs about ICSs and adherence.[18] Participants expressed fear of side effects and addiction from chronic medication; they relied on their assessment of asthma control and need for medications over that of the physician. Other personal obligations and prohibitive cost interfered with obtaining ICSs. Finally, distrust of the medical establishment also influenced adherence in these patients.

Adams et al[19] examined the effect of medical establishment characteristics on patient behavior in a population-based cross-sectional study examining the use of anti-inflammatory medications. Anti-inflammatory use was significantly associated with patients' perceptions of their physicians' abilities to explain asthma management well, making regular visits to a physician for asthma, and having a written asthma action plan. Additionally, patient social characteristics (being of white, non-Hispanic ethnicity; not missing work or school; and having a hospitalization for asthma in the past year) were associated with current self-reported use of anti-inflammatory medication.

Finally, Cisternas et al[20] examined the direct and indirect costs of asthma from a societal perspective in an ongoing community-based survey of 401 adults with asthma. Total person annual costs averaged $4912, with direct costs comprising 65% of these annual costs and 50% of the direct costs attributed to pharmaceuticals. The loss of work was the largest indirect cost.

Combining these findings, the studies suggest that both patient and medical establishment characteristics influence patient self-management, and these characteristics also influence each other. Patient adherence, a major component of self-management, is associated with their belief in the medication's efficacy and their assessment of the expertise of and satisfaction with their provider. Thus the method of asthma-care delivery influences patient self-management. Improving patient-physician interactions is one way self-management might be improved. Reducing the cost of these medications would also enhance adherence.

MANAGEMENT

Women's health

Asthma and pregnancy. Approximately 4% of pregnant women have a history of asthma.[21] Knowing more about asthmatic mothers' risks for morbidity as they enter pregnancy might improve management. Longitudinal studies are important for studying mother-child prognoses but are expensive and difficult to accomplish when the study period is long. Schatz et al[22] conducted a prospective cohort study by using a classification system modified from the 1993 National Asthma Education and Prevention Program Working Group that also incorporated the use of medications to study the relationship between asthma severity and gestational asthma exacerbations in pregnant asthmatic volunteers. The initial asthma severity classification was related to subsequent control of asthma during pregnancy measured on the basis of hospitalizations, urgent-care visits, oral corticosteroid use, and asthma symptoms during labor and delivery. However, 30% of women initially classified as having mild asthma were reclassified as having moderate-to-severe disease; 23% initially classified as having moderate-to-severe asthma were reclassified as having mild disease. Norjavaara and de Verdier[23] demonstrated the safety of budesonide in 2968 expectant mothers. Women gave birth to infants of normal gestational age, birth weight, and length. Although there was no increase in the numbers of stillbirths or multiple births, the rate of cesarian section was higher. Taken together, these studies warn clinicians to follow pregnant women with asthma cautiously and that ICSs are appropriate to control asthma.

Osteoporosis. High doses of ICSs might increase the risk of osteoporosis, particularly in groups who have other risk factors, such as postmenopausal state. Elmstahl et al[24] compared bone mineral densities in 106 postmenopausal Swedish women exposed to ICSs (88% to budesonide) with that of 674 similar women who were not exposed. Controlling for dietary differences and comorbidities, the study found no difference between bone densities in the ICS-exposed and unexposed groups, although the mean bone densities in another group exposed to systemic corticosteroids were lower. Stratifying on the basis of cumulative ICS dose, duration of therapy, and current dose greater than or less than 1000 μg revealed no difference between the exposed and unexposed groups. Although reassuring, the results must be interpreted cautiously because the study is cross-sectional rather than longitudinal.[25] Cross-sectional studies measure exposure (ICS) and disease (osteoporosis or bone density reading) at the same time point and cannot distinguish whether the ICS use preceded the develop-

ment of bone loss or whether bone loss (eg, caused by inactivity from asthma) affected the individual's level of exposure to ICSs. Additionally, the generalizability to other populations is not clear.

Therapy

Anti-IgE and immune-modulating drugs. In 2003, a monoclonal humanized anti-IgE antibody, omalizumab, was approved by the US Food and Drug Administration for the treatment of allergic asthma. Corren et al[26] analyzed data from phase III clinical trials of subjects 6 years and older and found reduced emergency department visits and hospitalizations over the year of treatment. Finn et al[27] conducted a 52-week, randomized, double-blind, placebo-controlled study of 525 adults and found improvement in asthma-specific quality of life. Other immune-modulating agents are under study. Sano et al[28] reported an improvement in the provocation concentration of histamine and a reduction in infiltrating eosinophils and $EG2^+$ cells associated with suplatast in 28 subjects, of whom 15 randomly received the drug for 6 weeks. Although these and other studies address the short-term efficacy and safety of these immune-modulating drugs, the long-term benefits and adverse effects remain to be identified. Postmarketing drug surveillance (phase IV studies) is essential.

Other therapies. Hughes et al[29] conducted a randomized placebo-controlled trial of 52 adults with severe exacerbations of asthma presenting to an emergency department in New Zealand and found the use of isotonic magnesium as an adjuvant to nebulized albuterol improved FEV_1 in the magnesium-treated group at 90 minutes. We will want to see further randomized controlled trials of this treatment. Considering prevention of exacerbations, Woodcock et al[30] conducted a randomized controlled trial of allergen-impermeable bed covers in adults with asthma who were sensitive to mites. After 6 months, mean morning peak expiratory flow rates did not differ between the groups. This and another article on the efficacy of such measures in the treatment of allergic rhinitis by Terreehorst et al[31] suggest that the myriad of elements that comprise patients' environments and the complexities in controlling patient exposures to diminish asthma morbidity are important research topics.

Allergic bronchopulmonary aspergillosis. Allergic bronchopulmonary aspergillosis, a hypersensitivity lung disease characterized by recurrent infiltrates and immune activation, sometimes accompanies asthma.[32] Because sensitivity to *Aspergillus* species antigens can be demonstrated in affected patients, *Aspergillus* species are hypothesized to be the causative agents. Treatment focuses on suppressing a hypersensitivity response to *Aspergillus* species antigens. Stevens et al[33] suggested that an antifungal agent, itraconazole, could provide synergistic benefit to corticosteroid therapy. Wark et al[34] conducted a randomized, double-blind, placebo-controlled trial of 400 mg of itraconazole administered daily in 29 stable patients. Patients in the itraconazole group had fewer exacerbations (median of 0 compared with 1.5, $P = .03$). Additionally, clinical markers of inflammation, sputum eosinophil counts, and serum IgE levels were lower in the treated group. This study lends support to the hypothesis that antifungal therapy is beneficial in allergic bronchopulmonary aspergillosis and alters the immune inflammatory response; however, larger prospective studies are needed.

ADVANCES IN PEDIATRIC ASTHMA

Our previous review concluded that "given the right medication and the patient profile, it may be possible to induce remission or even a cure."[2] The recent update to the National Asthma Education and Prevention Program Guidelines for the Diagnosis and Management of Asthma[35] addressed early intervention in young children and recommended long-term control therapy be considered for children with frequent episodes of asthma and a risk profile for persistent asthma. Recent *Journal* publications provide new insights on asthma development and management (Table II).

Asthma development

Children and their parents often ask whether they will outgrow asthma and whether asthma will return after remission. Rasmussen et al,[36] in a population-based, unselected birth cohort of 1037 New Zealanders, reported that sensitization to house dust mite, airway hyperresponsiveness, female sex, smoking, and early age of onset are associated with asthma persistence and relapse. Therefore early recognition and intervention could potentially alter the course of asthma.

Bager et al,[37] in a case-control study nested in an ongoing national cohort study, reported a positive association for the development of childhood asthma, but not allergic rhinitis, with maternal cesarean section. Chulada et al,[38] using data from the Third National Health and Nutrition Examination Survey, concluded that breast-feeding might delay the onset of or actively protect children less than 24 months of age against asthma and recurrent wheeze. As part of a larger prospective study of immunologic markers of asthma risk in the early years of life, Oddy et al[39] reported that increasing duration of breast-feeding was associated with decreasing prevalence of wheeze. The risk of wheeze was significantly decreased with increasing TGF-β1 dose from breast milk, suggesting a role for TGF-β1 in modifying asthma development.

In a birth cohort study from the Isle of Wight, Kurukulaaratchy et al[40] confirmed several findings previously mentioned as features associated with persistent wheezing. In children with BHR, current wheezers had higher total IgE levels and greater BHR than those who never wheezed. Symptomatic BHR at age 10 years was also associated with atopic sensitization and maternal asthma at 10 years of age in addition to parental smoking at 4 years of age. Gore et al[40a] investigated the relationship between urinary eosinophilic protein X and clinical phenotypes suggestive of allergic diseases in older children. They concluded that urinary eosinophilic protein X reflects the

presence of atopy and associated symptoms and might be useful for monitoring the progression of allergic disease.

In regard to environmental exposure, considering the indoor environment, Rullo et al[41] analyzed dust from daycare centers, preschools, kindergartens, and elementary schools. They concluded that daycare centers and schools in Brazil should be considered as important sources of exposure to dust mites and cockroach allergens and endotoxin. Werner et al[42] investigated whether the effect of endotoxin concentration in house dust on asthma is modified by the presence of variation in the *TLR4* gene. In the noncarrier group the prevalence of asthma was significantly increased with increased endotoxin levels in house dust. The carriers of the polymorphisms showed a nonsignificant trend toward a lower risk of asthma. They found a similar association for wheeze and endotoxin exposure that was also attenuated in subjects with G299/1399 polymorphisms. Looking outdoors, there were at least 2 articles associating the asthma morbidity with exposure to ozone[43] and nitrogen dioxide[44] in children. The effect of both indoor and outdoor exposures on the respiratory system deserves further attention.

Litonjua et al[45] reported that exposure to high concentrations of house dust endotoxin of greater than the median level was associated with an increased risk for wheezing in young children, but the risk rapidly decreased over time. Exposure to cockroach allergen was associated with increased risk for wheezing, whereas exposure to cat allergen and the presence of a dog in the home were both associated with decreased risk for wheezing. Svanes et al[46] reported that keeping cats in childhood was associated with asthma only among atopic subjects and was stronger where cats were less common. Dogs owned in childhood or adulthood were associated with asthma among nonatopic subjects. Among atopic subjects, those who had owned dogs in childhood had less hay fever and no increased risk of asthma. Respiratory symptoms were more common in subjects who had owned birds during childhood, independent of sensitization.

Regarding bacterial infection, Medeiros et al[47] concluded that *Schistosoma mansoni* infection was associated with a milder course of asthma. Nagy et al[48] investigated the role of *Chlamydia pneumoniae* infection in children with asthma and the modifying effect of mannose-binding lectin variant alleles. They concluded that there was an important role of variant mannose-binding lectin alleles in the susceptibility to asthma in children infected with *C pneumoniae*. Bager et al[49] reported that smallpox vaccination was associated with a slightly decreased risk of asthma but no association with risk of atopy or allergic rhinitis.

Regarding viral infection, Kotaniemi-Syrjanen et al[50] concluded that rhinovirus infections are important inducers of wheezing even in infancy and should be evaluated for their role in the development of asthma. Kim et al[51] reported that a subgroup of the respiratory syncytial virus–induced bronchiolitis group results in a T_H2-type response, and this could provide a link between respiratory syncytial virus–induced bronchiolitis and asthma.

These fascinating articles focus on the importance of understanding the interaction between environment and genome, as do some of the articles described earlier. Further investigation will depend on good clinical definitions and rigorous observational and intervention studies, not an easy task because the latency between risk factor and end point is long in many cases. Future studies will also require close collaboration of basic scientists and clinical researchers.

Asthma pathology

Relatively little new information has appeared in this area for children; however, Nakano et al[52] reported that levels of plasma C3a, a complement component and anaphylotoxin, were increased in patients with acute asthma exacerbations and was reduced with asthma therapy. Jenkins et al[53] reported on a case series of children with difficult-to-control asthma who underwent diagnostic bronchial biopsies. Despite little evidence of ongoing airway inflammation, many of the patients had significant lung function lability, suggesting varying forms of steroid resistance, such as distal airways inflammation or remodeling insensitive to steroids.

Objective measures

Marotta et al[54] evaluated impulse oscillometry as a measure of lung function in young children and reported that asthmatic patients differed significantly in their impulse oscillometry–assessed bronchodilator responses through change in resistance. Anderson et al[55] evaluated the increase in the number and percentage of athletes competing in Olympic Games requesting use of β_2-agonists for asthma. They concluded that assessment for a reduction in FEV_1 or a certain level of airway hyperresponsiveness was feasible and helpful for screening athletes.

Strunk et al[56] reported that eNO was significantly correlated with peripheral blood eosinophils, IgE, and serum eosinophilic cationic protein but not with urinary leukotrienes and moderately correlated with the number of positive aeroallergen skin test responses. However, eNO showed no to weak correlation with pulmonary function measures, including airway hyperresponsivenes. Therefore it might provide supplementary information for asthma assessment.

Behavior intervention

Strunk et al[57] reported that adherence and retention problems in long-term follow-up in the Childhood Asthma Management Program increased with the duration of participation, increasing child age, and the presence of less family cohesion or attention problems in the child. Calam et al[58] reported that children at age 3 years with symptoms suggestive of asthma are at increased risk of behavioral problems. Children with families without a history of asthma and allergic diseases might be particularly vulnerable to behavioral disturbance.

Roberts et al[59] developed and validated a health-related quality-of-life measure that included problems related to the eyes, ears, nose, lungs, skin, emotions, and everyday

activities, proposing it as a potentially useful outcome measure in the evaluation of treatment effects in children with multisystem allergic disease. Ho et al[60] concluded that the construction of a simple self-report asthma knowledge instrument for use as a primary outcome measure might not be feasible because the reliability testing was poor, there was no association between asthma knowledge and treatment adherence or outcomes, and asthma knowledge was not a simple function of education. Sullivan et al[61] found that a comprehensive social worker–based asthma-intervention program and environmental control reduced symptom days and was cost-effective for inner-city children with asthma, especially those with more severe disease.

ICSs

ICSs are recognized as the preferred long-term controller for all levels of persistent asthma and in all age groups, including young children.[35,62] The recent report of the START study confirmed the beneficial effects of preventing severe exacerbations and improving overall asthma control with low-dose ICSs in recent-onset, mild, persistent asthma in adults, as well as in children greater than 5 years of age.[63] Schatz et al[64] reported that dispensing of 7 or more canisters of ICSs per year was associated with reduced subsequent emergency asthma hospital use. Cost-effectiveness analyses will be important subsequent studies.

Busse et al[65] found that combination therapy, fluticasone propionate (FP) and salmeterol in the Diskus device administered twice daily, allowed a 60% reduction in the FP dose while maintaining overall asthma control in children 12 years of age and older. Nelson et al[66] reported that this combination therapy formulation offers the potential for increased clinical efficacy, as indicated by improvement in pulmonary function, over concurrent use of the same doses of the 2 drugs in separate devices.

Wong et al[67] reported that infants are likely to inhale approximately 8% of the nominal dose of FP inhaled from a spacer device (Babyhaler) with face-mask attachment. Allen et al[68] provided a comprehensive review of the current status of ICSs in asthma therapy efficacy and safety, as well as areas that could be improved with ICS delivery to the airways.

Montelukast

This medication was identified as an alternative to ICSs in patients with mild persistent asthma and supplementary therapy to ICSs for patients with moderate persistent asthma.[62] Israel et al[69] reported that the percentage of asthma control days was almost identical between the montelukast and low-dose ICS groups, with both being greater than in patients treated with placebo; however, the ICSs had a greater effect on improving FEV_1. Meyer et al[70] were not able to identify any patient characteristics associated with a response to montelukast in children. Melo et al[71] observed that once-daily treatment with montelukast in asthmatic children attenuated the immediate-phase response and ablated the late-phase response induced by exercise.

CONCLUSIONS

The allergy and immunology community is strongly committed to research to improve health care education, delivery, and quality. Increasingly, investigations involve collaborations of basic scientists, geneticists, and clinical researchers, as evidenced in the studies from around the world that are reviewed here. For example, understanding the effect of environment and genes on illness involves careful definition and measurement of clinical risk factors as these constructs become the basis for genomic analyses and the identified gene products are studied for their contribution to disease. In addition, understanding approaches to disease management from the patient, provider, and societal perspectives; understanding the effect of society on health; and understanding communication between providers and patients after beneficial and adverse effects of new drugs as our experience with them increases all require careful clinical research. Early recognition and early intervention for childhood asthma is a topic of great interest, and new information is forthcoming at a rapid pace. This information must be carefully integrated into health care systems to optimize benefits and minimize any risk of adverse effects. The American Academy of Allergy, Asthma and Immunology has a new interest section, now called “Health Care, Education, Delivery and Quality,” and with this issue, the JACI will devote a section to clinical and health services research. It is anticipated that this section of the JACI will serve as a center for discussion and collaboration from the worldwide community of scientists on all aspects of allergy and immunology that involve clinical research.

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