Advances in pediatric asthma in 2009: Gaining control of childhood asthma

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This year's summary will focus on recent advances in pediatric asthma as reported in *Journal of Allergy and Clinical Immunology* publications in 2009. New National Asthma Education and Prevention Program asthma guidelines were released in 2007, with a particular emphasis on asthma control. Now that we have worked with the principals of the guidelines for 2 years, new insights are reported on how to implement the guidelines into clinical practice. This year's report will focus on gaps in management that need to be addressed, including health disparities, methods to improve asthma management through opportunities available in school-based asthma programs, and more information on the development of asthma in childhood. This information brings us closer to the point of managing children with controllable asthma and understanding reasons why asthma is not controlled in the remaining children. If we can close these gaps through better communication, improvements in the health care system, and new insights into treatment, we will move closer to better methods to intervene early in the course of the disease and induce clinical remission as quickly as possible in most children. (J Allergy Clin Immunol 2010;125:69-78.)

Key words: *Asthma, asthma control, asthma impairment, asthma risk, asthma severity, early intervention in asthma, biomarkers, genetics, inhaled corticosteroids, leukotriene receptor antagonists, long-acting β-adrenergic agonists, omalizumab, therapeutics*

Abbreviations used

AAAAI:	American Academy of Allergy, Asthma & Immunology
AHR:	Airway hyperresponsiveness
BMI:	Body mass index
FeNO:	Fraction of exhaled nitric oxide
FLG:	Filaggrin
FSC:	Fluticasone propionate–salmeterol combination
FSE:	Future severe exacerbation
HLX1:	Homeobox transcription factor H.20-like homeobox 1 gene
ICS:	Inhaled corticosteroid
LABA:	Long acting β-adrenergic agonists
LTRA:	Leukotriene receptor antagonist
NAEPP:	National Asthma Education and Prevention Program
OR:	Odds ratio
PLAUR:	Plasma urokinase plasminogen activator receptor
RI:	Rhode Island
RSE:	Recent severe asthma exacerbation
RSV:	Respiratory syncytial virus
TBX21:	T-cell specific T-box transcription factor
TSLP:	Thymic stromal lymphopoietin

Last year's summary in this "Advances in pediatric asthma" series included a discussion of elements that would be necessary to implement the asthma guidelines, such as focusing on asthma control in adjusting therapy, applying techniques from managed asthma care to understand populations at risk for poor control, identifying early indicators of developing asthma, anticipating asthma exacerbations, and monitoring progression.[1] That summary ended with some thoughts regarding the introduction of personalized medicine to asthma care for children.

This review will highlight 2009 *Journal of Allergy and Clinical Immunology* publications that provide new information pointing to breakdowns in asthma care that require solutions, the opportunities available to implement school-based asthma programs, and new information that will help us understand the development of asthma in children.

CORE PRINCIPLES OF THE ASTHMA GUIDELINES

The 2007 version of the National Asthma Education and Prevention Program (NAEPP) Expert Panel Report 3 emphasized the importance of asthma control, a stepwise approach to asthma management, and the importance of early diagnosis and intervention.[2,3] The new NAEPP asthma guidelines introduced several new terms to apply to asthma management, specifically *assessment of severity*, *control*, *responsiveness*, *impairment*, and *risk*.[2,3] Severity is defined as the intrinsic intensity of the disease process. Control is the degree to which the manifestations of asthma (symptoms, functional impairment, and risks of untoward events) are minimized and the goals of therapy are achieved. Responsiveness is the ease with which control is achieved by therapy.

Asthma severity and asthma control are both divided into 2 domains: impairment and risk. Impairment is the assessment of the frequency and intensity of symptoms, as well as the functional

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limitations that the patient is experiencing now or in the past because of his or her asthma. Risk is the estimate of the likelihood of an asthma exacerbation, progressive loss of pulmonary function over time caused by asthma, or an adverse event caused by medication or even death. The assessment of severity and control provide guidance on the direction to take in conducting additional diagnostic evaluation, assessing environmental factors and adherence to the management plan, and consequently stepping up or stepping down medications.

ASTHMA CONTROL: BREAKDOWNS AND POTENTIAL SOLUTIONS

Asthma exacerbations

Several publications emerging from the Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens Study highlight some important features of poorly controlled asthma. The recent publications focused on information derived from the pediatric component of this study. One area of analysis evaluated whether the level of impairment, as defined by the 2007 asthma guidelines, predicts the risk for future asthma exacerbations.[4] Children aged 6 to 11 years and adolescent/adult patients aged 12 years or older were examined on entry into the study and at months 12 and 24. This study reported that children with consistently very poorly controlled asthma over the 2-year period demonstrated a 6-fold increased risk of hospitalization, emergency department visit, or corticosteroid burst (odds ratio [OR], 6.4) compared with the group that improved over the same time period. Adolescent/adult patients with consistently very poorly controlled asthma were more likely to have a corticosteroid burst (OR, 2.8) or have a hospitalization, emergency department visit, or corticosteroid burst (OR, 3.2). They concluded that consistently very poorly controlled asthma is strongly predictive of future asthma exacerbations.

Another study from this group investigated the risk of future severe exacerbations (FSEs) in children with severe/difficult-to-treat asthma and recent severe asthma exacerbations (RSEs).[5] In a multivariate model FSEs at 6 months after enrollment were most strongly associated with RSEs (OR, 3.08) and having 3 to 4 allergic triggers (OR, 2.05). Race (OR, 1.77) and very poorly controlled symptoms (OR, 1.59) also significantly predicted FSEs. Therefore RSEs are an important independent predictor of FSEs in children with severe/difficult-to-treat asthma and should be considered when setting up management plans.

Health disparities

The June *Journal of Allergy and Clinical Immunology* theme issue was focused on asthma disparities, and several reviews provided important observations to consider for improving asthma care. Bryant-Stephens[6] points out that asthma continues to disproportionately affect minority and low-income groups, with African American and Latino children who live in low-socioeconomic-status urban environments experiencing higher asthma morbidity and mortality than white children. She points out that because asthma is a complex disease that affects millions of persons, multifaceted comprehensive interventions that combine all evidence-based successful strategies are essential to finally closing the gap in asthma morbidity. Canino et al[7] also make the point that a multilevel framework for integrating research in health disparities is needed to advance both future research and clinical practice. They propose that several strategies that could be applied in clinical settings to reduce asthma disparities include the need for routine assessment of the patient's beliefs, reduction of financial barriers to disease management, and health literacy and the provision of cultural competence training and communication skills to health care provider groups.

Valet et al[8] indicate that 21% of the US population lives in rural areas. Rural populations have lower income, a higher rate of government versus private insurance, and decreased access to health care compared with persons living in urban areas. Unfortunately, there has been little research on asthma prevalence and severity in rural US populations compared with that on other international populations. Future work is needed to more clearly define asthma prevalence and morbidity among residents of the rural United States, as well as to identify interventions effective in this population.

In an editorial to this theme issue, Apter and Casillas[9] point out that the American Academy of Allergy, Asthma & Immunology (AAAAI) has made a number of efforts to reduce health disparities through Academy CAN! by pairing an allergist/asthma specialist with a community clinic in an underserved area. The AAAAI has also been a member of the Commission to End Health Disparities since its origin in 2004. The AAAAI has several programs in place to try to remedy the problem of a shortage of minority providers underrepresented in medicine, including the Chrysalis Project, the Odyssey Program, and the Fellowship of Excellence Award, as well as developing a partnership with the National Medical Association. However, they also point out that there is much more to do not only to reduce health disparities nationally but also to take a more global approach to address inequities around insurance coverage as part of health care reform.

Community factors

Another important way to look at asthma control is to look at individual populations and to examine ways that might be inherent in the environment or culture that could contribute to poor asthma control or enhance asthma control. Gruchalla et al[10] evaluated the role of various indicators to predict future asthma control in an inner-city population aged 12 through 20 years enrolled in a National Institute of Allergy and Infectious Diseases Inner City Asthma Consortium study that applied a guidelines-based approach to asthma care. Surprisingly, they found that the usual predictors of future disease activity have little predictive power when applied to a highly adherent population with persistent asthma that is receiving guidelines-based care. Therefore they believed that new predictors need to be identified that will be able to measure the continued fluctuation of disease, such as asthma exacerbations and periodic episodes of loss of control, that persists in highly adherent, well–treated populations, such as the one studied.

It is well recognized that managing asthma in adolescence is a challenge, particularly for children in the inner-city environment. Naimi et al[11] sought to describe adherence to preventative asthma medications and explore relevant beliefs and attitudes, as well as to seek out ideas for improving adherence from inner-city youth. As expected, they found that adherence was poor and concluded that examining and acknowledging health beliefs of older teens in the context of their life structure could facilitate discussions about self-management. Some of the beliefs from subjects included the feeling that taking the medications was not necessary, and some of them even doubted their benefit.