



Pediatric asthma – moving ahead faster than ever

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In the past 35 years, emphasis has been placed on consolidating information around asthma in the form of guidelines. These initially developed as country-specific guidelines but over time emerged into global strategies, specifically the Global Initiative for Asthma (GINA) [1], with periodic updates to national guidelines. Gaps in information identified by guidelines committees have prompted research to fill those gaps. Fortunately, children have benefitted from this set of events as prior to the year 2000, there was very little evidence obtained in children to guide the management of childhood asthma. Looking at the past 50 years in the evolution of current asthma management, one can see a paradigm shift about every 10 years (Table 1).

The ongoing evolution of asthma management has resulted from an interplay between clinicians identifying areas of need and the pharmaceutical industry responding by developing new medications to address those needs. Noteworthy is that in a period of 15 years, there was only one new medication introduced, namely anti-IgE, but in the past 2 years, there have been three new classes of medications introduced, including tiotropium, a long-acting anticholinergic inhaled medication, two forms of anti-IL5, specifically, mepolizumab and reslizumab, as well as the approval of bronchial thermoplasty, although the latter two only currently approved for use in patients 18 years of age and older. There are a number of new medications being developed that could be potentially introduced in the next 5 years, such as anti-IL4/13 (dupilumab) and other immunomodulators [2].

Introduction of new medications and procedures prompt questions related to the appropriate use of these new strategies as well as their application in children. The past 10 years has seen a shift toward an emphasis on achieving and maintaining asthma control. The next 10 years will see a focus placed on incorporating new strategies of population health to identify children at risk for asthma exacerbations as well as the onset of asthma, using patient-specific phenotypic characteristics to decide upon optimal treatment strategies, and utilizing new forms of management to prevent asthma exacerbations, progression of the disease, and ultimately asthma onset.

CURRENT KNOWLEDGE AND ROLE OF ASTHMA GUIDELINES: POTENTIAL LAG IN APPLYING EVIDENCE-BASED MEDICINE

Becker and Abrams [3] present a review of the similarities and differences between the GINA Global Strategy for Asthma Management and Prevention and the various sets of national guidelines that are available. They point out that GINA is a strategy that is updated on annual basis with ongoing review of the literature. It is designed to serve as a template for the development of national guidelines. Contrary to GINA, national guidelines are updated periodically and may span as long as 10 years as typified by the National Asthma Education and Prevention Program guidelines that were last updated in 2007 and are currently in the process of being updated [4]. There are various reasons for delays in updating national asthma guidelines that may be related to costs involved in producing updates, the need to form expert panels, and the accumulation of sufficient new information to merit an update. Clinicians must abide by their own national asthma guidelines as they take into consideration the medications available in that particular country and the regulatory bodies that approve the use of such medications. Therefore, the national guidelines serve as the base for practice in individual countries, whereas GINA serves as a resource to draw upon regularly updated information.

NEW KNOWLEDGE REGARDING ASTHMA ONSET AND OUTCOMES OF CONCERN

There have been ongoing discussions on whether childhood asthma can develop into an irreversible

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Table 1. Evolving patterns in asthma management

Period	Goal of management	Medications
1960s	Relieve bronchospasm	Short-acting β -agonists
1970s	Prevent bronchospasm	Albuterol, theophylline
1980s	Prevent allergen-induced bronchospasm	Cromolyn
1990s	Prevent and resolve inflammation	ICS, LT modifiers, LABA, ICS/LABA
2000s	Asthma control	Anti-IgE
2010s	Personalized medicine; prevention strategies	Tiotropium; anti-IL5; bronchial thermoplasty; technology
2020s	Population health management	Individualized treatment strategies

ICS, inhaled corticosteroids; LT, leukotriene; LABA, long-acting beta-agonist.

form of respiratory disease similar in presentation to chronic obstructive pulmonary disease. McGeachie [5] reviews the results of the recently published outcomes of the National Heart, Lung and Blood Institute Childhood Asthma Management Program that began enrollment in 1991. Over 1000 children, aged 5–12 years, with mild-to-moderate asthma were enrolled in this study between 1992 and 1994 and treated over at least a 5-year period with three different management strategies, including daily inhaled corticosteroid therapy. Following common completion of the study period in 1999, these children were followed into young adulthood to assess long-term outcomes related to linear growth as well as lung function over time. Consequently, there were four different patterns of lung function development that emerged over time. Of concern was that approximately one-half of the population had evidence of reduced lung function in childhood that persisted over time with about half of this population showing further loss of lung function with time. Even in those with normal lung function during the course of development in childhood, approximately 50% of that population showed loss of lung function in early adulthood. This observation prompts questions related to the cause for loss in lung function and methods to prevent this loss.

Rosas-Salazar and Hartert [6] discuss potential modifiable prenatal exposures that appear to be associated with childhood wheezing illness, including parental smoking, outdoor air pollution, and maternal stress. However, the role of many other prenatal exposures on the onset of childhood wheezing illnesses remains unclear. Anderson and Jackson [7] discuss the interplay between genetic predisposition and environmental exposures, including allergens and microbes. They conclude that interventions aimed at these risk factors during the preschool years may prevent the longitudinal course of asthma progress to irreversible airway obstruction. In addition, Forno and Celedon [8] reviewed the evidence regarding the relationship of obesity and asthma. They

conclude that obesity increases the risk of asthma and worsens asthma severity or control via multiple mechanisms. Therefore, obesity and its complications must be managed as an integral part of asthma treatment in obese children.

CURRENT AND FUTURE MANAGEMENT OF ASTHMA

Besides managing obesity and various exposures, new strategies will be needed to prevent asthma progression and the consequences of asthma exacerbations and it must begin in early childhood. Beigelman and Bacharier [9] address the management of recurrent wheezing and asthma in early childhood. They propose a phenotype-based strategy as certain young children are likely to benefit from daily inhaled corticosteroid therapy in reducing the risk of asthma exacerbations. These children have allergen sensitivity or high blood eosinophils. In addition, targeting airway bacteria has emerged as a promising therapeutic approach, although further studies are needed to assure that antibiotic resistance is not a significant consequence of this approach.

Lee-Sarwar *et al.* [10] review strategies that may alter the natural history of childhood asthma. As the presentation of asthma may be very heterogeneous, it is important to identify risk factors for asthma occurrence, persistence, and severity to guide efforts to alter the natural history of asthma. Several promising strategies include vitamin D supplementation and air pollution reduction that merit increased investigation and implementation. With the implementation of these strategies, asthma management in young children will likely differ in the future, as summarized by Burbank and Szeffler [11]. It will be important to establish the phenotype and endotype of young wheezing children to be able to prognosticate future asthma risk. This will also be helpful in the selection of the most appropriate asthma treatment. Primary asthma prevention strategies are needed during the critical developmental window

in early life prior to the onset of irrecoverable loss of lung function.

MANAGEMENT STEPS FOR IMMEDIATE APPLICATION

As we await the refinement of phenotyping and endotyping strategies, certain steps can be taken immediately to reduce asthma morbidity. The application of technological innovations, including text messaging, smart phone applications, and electronic monitoring devices can be aimed at improving asthma controller adherence as reviewed by Anderson [12]. These advances in technology can augment medication adherence but further studies are needed to investigate their clinical impact as they are implemented in clinical practice.

In addition, school nurses are an underutilized member of the healthcare team. They should be able to play a vital role in supporting the asthma management plan. Kakumanu and colleagues [13] summarize the development of the American Academy of Allergy, Asthma and Immunology and National Association of School Nurses collaborative to form a School-Based Asthma Program (SAMPRO). This program is readily available to clinicians and school nurses to partner more effectively in the management of childhood asthma. Hopefully, new directions in the healthcare system will provide the necessary resources for school nurses to expand their role in chronic disease management, including asthma and thus minimize school absence because of chronic disease and consequently optimize academic achievement.

FUTURE PERSPECTIVE

Our goal in this section is to provide a series of articles that summarize the ongoing changes that are likely to occur with asthma management as we recognize the characteristics of children likely to develop asthma, those that are at risk to progress during the course of the disease, and those that will emerge to develop severe asthma. Hopefully, intervention with new treatment strategies, including new ways to monitor the course of asthma, identification of

phenotypes and endotypes at risk for asthma exacerbations and severe asthma, better utilization of available medications, development of new immunomodulator therapies, and the incorporation of new technologies and new support systems will serve to reduce the risk of asthma exacerbations. These strategies should also serve to reduce the risk for the development of asthma into long-term outcomes of chronic obstructive pulmonary disease.

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REFERENCES

1. Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2015. Available: <http://www.ginasthma.org/>. [Accessed 14 March 2016]
2. Anderson WC 3rd, Szeffler SJ. New and future strategies to improve asthma control in children. *J Allergy Clin Immunol* 2015; 136:848–859.
3. Becker AB, Abrams EM. Asthma guidelines: the Global Initiative for Asthma in relation to national guidelines. *Curr Opin Allergy Clin Immunol* 2017; 17:99–103.
4. National Asthma Education and Prevention Program. Expert panel report 3 (EPR-3): guidelines for the diagnosis and management of asthma-summary report 2007. *J Allergy Clin Immunol* 2007; 120 (5 Suppl):S94–S138.
5. McGeachie MJ. Childhood asthma as a risk factor for the development of chronic obstructive pulmonary disease. *Curr Opin Allergy Clin Immunol* 2017; 17:104–109.
6. Rosas-Salazar C, Hartert TV. Prenatal exposures and the development of childhood wheezing illnesses. *Curr Opin Allergy Clin Immunol* 2017; 17:110–115.
7. Anderson HM, Jackson DJ. Microbes, allergic sensitization, and the natural history of asthma. *Curr Opin Allergy Clin Immunol* 2017; 17:116–122.
8. Forno E, Celedón JC. The effect of obesity, weight gain, and weight loss on asthma inception and control. *Curr Opin Allergy Clin Immunol* 2017; 17:123–130.
9. Beigelman A, Bacharier LB. Management of preschool recurrent wheezing and asthma: a phenotype-based approach. *Curr Opin Allergy Clin Immunol* 2017; 17:131–138.
10. Lee-Sarwar KA, Bacharier LB, Litonjua AA. Strategies to alter the natural history of childhood asthma. *Curr Opin Allergy Clin Immunol* 2017; 17:139–145.
11. Burbank AJ, Szeffler SJ. Current and future management of the young child with early onset wheezing. *Curr Opin Allergy Clin Immunol* 2017; 17:146–152.
12. Anderson WC. Incorporating technology to advance asthma controller adherence. *Curr Opin Allergy Clin Immunol* 2017; 17:153–159.
13. Kakumanu S, Antos N, Szeffler SJ, Lemanske RF. Building school health partnerships to improve pediatric asthma care: the School-based asthma Management Program. *Curr Opin Allergy Clin Immunol* 2017; 17:160–166.