

A white paper on evolving asthma therapy

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Primary Care Management of Patients With Asthma

LEARNING OBJECTIVES

After reviewing this activity, the reader will be better able to:

1. Describe the role of asthma severity in initiating therapy and that of asthma control in adjusting therapy.
2. Describe the evolving evidence regarding the role of small- and large-airway inflammation in asthma.
3. Describe the appropriate use of long-acting inhaled β -agonists (LABAs) in patients with persistent asthma.
4. Describe how better physician-patient communication and the use of a written asthma action plan (WAAP) can help improve patient self-management.

TARGET AUDIENCE

Family physicians and clinicians who are interested in gaining increased knowledge and a stronger competency regarding evolving considerations in the primary care management of patients with asthma.

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The Primary Care Education Consortium clinical staff have provided financial disclosure and have no conflicts of interest to resolve related to this activity.

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Introduction

Seventy-one percent—that's the percentage of patients with asthma who participated in the 2009 Asthma Insight and Management (AIM) survey and reported that their asthma symptoms during the past 4 weeks were completely or well controlled.¹ Only 6% reported that their asthma symptoms were poorly or not controlled.¹ Yet when the criteria for asthma control from the 2007 National Asthma Education and Prevention Program (NAEPP) Expert Panel Report 3 (EPR3): Guidelines for the Diagnosis and Management of Asthma² were applied, only 29% of patients surveyed had asthma that was well controlled.¹ In fact, nearly half of patients surveyed—47%—had asthma that was very poorly controlled.¹

The 2009 AIM survey also showed that compared to the 1998 Asthma in America survey, only modest decreases were observed in the need for acute care, the number of days of work/school missed, or limitations on activity.¹ The AIM survey also found that 39% of patients believed that maintenance treatment was not necessary when asthma symptoms were not experienced regularly, while 67% believed that rescue medications can be used every day if needed.¹

These measures indicate that there has been little improvement over the past decade in the impact of asthma on patients. It appears, therefore, that there is considerable opportunity for improved patient self-management, as patients with asthma do not recognize, or are willing to accept, frequent asthma-related morbidity. Further, there seems to be a lack of understanding among patients about the central role of inflammation in asthma and the importance of daily controller therapy.

This review seeks to address these issues and focuses on: 1. impairment and risk domains as guides to initiating and modifying treatment; 2. the role of inflammation in asthma, including inflammation of the small airways; and 3. the appropriate role of long-acting inhaled β -ago-

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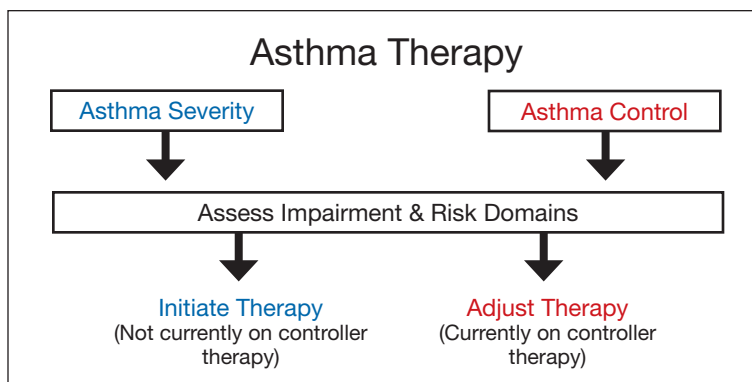
nists (LABAs) and recent actions by the US Food and Drug Administration (FDA) concerning their use. Considerable attention is paid to physician-patient communication, as well as written asthma action plans (WAAPs), their components, and tips for their use as a means of improving patient self-management.

Impairment and Risk Domains

Assessment of the impairment and risk domains is recommended by the NAEPP EPR3 to determine the severity of disease in patients who are not on long-term-control treatment before treatment is initiated, or the level of control that has been achieved after treatment has been initiated (FIGURE 1).² Asthma severity is defined by the NAEPP as the intrinsic intensity of the disease process, while control is the degree to which the manifestations of asthma (ie, symptoms, functional impairment, and risks of untoward events) are minimized and the goals of therapy are met. Assessment of the impairment domain includes the frequency and intensity of symptoms and functional limitations a patient is experiencing or has recently experienced. Specific measures within the impairment domain include nighttime awakenings, use of short-acting inhaled β -agonists (SABAs), interference with normal activity (work/school and normal/desired activities), and results of pulmonary function tests (spirometry, peak expiratory flow).² Validated questionnaires are also used to assess impairment and are available in both English and Spanish (TABLE 1).

While the impairment domain considers the recent past and present, the risk domain estimates the likelihood of future adverse events, including exacerbations requiring oral systemic corticosteroids and progressive, irreversible loss of pulmonary function.² Preventing reduction in lung growth in children and minimizing or preventing treatment-related adverse effects are also considered. To estimate risk, the risk domain considers a patient's medical history and the need for unscheduled office visits, emergency department visits, hospitalizations, intubation, and admission to the intensive care unit over the past year. Spirometry, which determines forced expiratory volume in 1 second (FEV₁) expressed as a percentage of the predicted value, or as a proportion of the forced vital capacity (FVC)—FEV₁/FVC—is the most useful test for predicting risk of future events.²

FIGURE 1 Initiating and adjusting asthma therapy based on impairment and risk domains²



Let's consider 2 cases in the context of impairment and risk.

Case 1

- 7-year-old female diagnosed with mild persistent asthma at age 3 years
- Current assessment of asthma control:
 - FEV₁, 68% of predicted; FEV₁/FVC, 72%
 - Often feels short of breath during gym class or when playing outdoors; responds to SABA (uses more than twice a week)
 - Experiences 3 to 4 nighttime awakenings per month
 - Experiences an exacerbation every 3 to 4 months that requires nebulized albuterol in the office or emergency department
 - Childhood Asthma Control Test (C-ACT) score, 15
- Presently treated with montelukast and prn SABA

Case 2

- 25-year-old female diagnosed with asthma at age 6 years
- Moved to an older inner-city apartment building 7 months ago
- Current assessment of asthma control:
 - FEV₁, 65% of predicted; FEV₁/FVC, 74%
 - Mild shortness of breath at least 3 to 4 times per week and 2 to 3 nighttime awakenings per month, both of which respond to SABA
 - Experienced 2 exacerbations in the past 6 months that required nebulized albuterol in the office or emergency department
 - Asthma Control Test (ACT) score, 17
- Presently taking a low-dose inhaled corticosteroid (ICS) and prn SABA

Based on signs, symptoms, pulmonary function, and SABA use, both patients have asthma that is not well controlled. An ACT or C-ACT score ≤ 19 also indicates asthma that is not well controlled. When considering changing a patient's treatment plan, it is important to take into account factors that may affect control; for example, treatment adherence should be investigated and barriers to adherence addressed. The patient should be asked to demonstrate his or her inhaler technique, with proper technique demonstrated by the clinician, if needed. Environmental factors that may contribute to poor control should also be investigated with a detailed history and an appropriate allergy workup, including either skin prick or in vitro testing. Treatment should be modified, as appropriate, based on these findings.

Treatment

The treatment of patients with asthma continues to evolve as more is learned about its pathogenesis and more experience with treatment options is gained.

Pathogenesis of asthma: Inflammation

The central role of inflammation of the large airways in the pathogenesis of asthma is clearly established² and typically is the focus of treatment for persistent asthma. The contribution of small (distal)-airway inflammation to the pathogenesis of asthma may be less appreciated but has been demonstrated in autopsy specimens.⁷ Structural changes within the alveoli, such as alveolar walls that extend radially from the outer wall of the non-respiratory bronchiole and decreased elastic fiber content, have been observed.⁸ Two decades ago, Wagner et al measured pressure-flow relationships in 6 healthy subjects and 9 subjects with asymptomatic asthma.⁹ While spirometry detected no differences in lung function between the 2 groups, peripheral lung resistance was found to be increased more than 7-fold in asthmatic subjects compared to healthy subjects. Subsequent investigation by the same investigators demonstrated a doubling of peripheral lung resistance at lower average histamine concentrations in subjects with asthma compared to healthy subjects, correlating with whole lung responsiveness in subjects with asthma.¹⁰

Aerosolized medications: Inhaled corticosteroids

While the importance and role of the small airways in asthma pathogenesis continue to be investigated, increased attention on small-airway inflammation in asthma has spawned interest in the particle size of aerosolized medications for metered-dose inhalers such as ICSs. Most ICS particles in a chlorofluorocarbon (CFC) formulation, which is no longer available, had a mean diameter of 3.5 μm to 4.5 μm , which limited their penetration into the ≤ 2 - to 3- μm diameter of the small airways.¹¹ On the other hand, ICS particles in hydrofluoroalkane (HFA) formulations, which have a mean diameter of about 1 μm , have been shown to have a higher deposition rate into the small airways.^{12,13} A deposition rate of 53% has been demonstrated for HFA-beclomethasone dipropionate (BDP) compared to 12% to 13% for CFC-fluticasone propionate (FP) and 4% for CFC-BDP.¹²

The generally greater deposition into the small airways of HFA ICS compared to CFC ICS may be an important consideration in patient management, provided that the smaller particle size of the HFA ICS has a favorable impact on disease progression or pathophysiology, greater improvement in symptoms, or improved safety/tolerability. At present, the evidence must be considered preliminary. Significant improvement in small-airway resistance over 12 weeks compared to baseline has been observed with HFA-BDP 200 μg daily ($P=.0003$).¹⁴ From a clinical perspective, improvement in FEV₁ compared to baseline has been observed with HFA-BDP at doses of 100 μg , 400 μg , or 800 μg daily ($P=.09$) over 6 weeks.¹⁵

TABLE 1 Validated questionnaires for assessing asthma impairment

Asthma Control Test (ACT)³ http://www.asthmacontrol.com/pdf/ACT_AdultEng.pdf http://www.asthmacontrol.com/pdf/ACT%20AdultPageSP.pdf
Childhood Asthma Control Test (C-ACT)⁴ http://www.asthmacontrol.com/pdf/BiChildEng.pdf http://www.asthmacontrol.com/pdf/BiChildSP.pdf
Asthma Therapy Assessment Questionnaire (ATAQ)⁵ http://www.asthmacontrolcheck.com/asthma_control/asthmacontrolcheck/consumer/index.jsp?WT.sv1=1
Asthma Control Questionnaire (ACQ)⁶ http://www.qoltech.co.uk/acq.html

Similar results have been observed with HFA-flunisolide 85 µg, 170 µg, or 340 µg twice daily over 12 weeks¹⁶ and HFA-ciclesonide 160 µg once daily over 12 weeks.¹⁷ A retrospective analysis of “real world” use of HFA-BDP compared to HFA-FP or CFC-FP demonstrated asthma control (ie, no unplanned visits or hospitalization for asthma, no prescription for oral corticosteroids, and no antibiotics for lower respiratory tract infection) in >80% of patients in each group over 1 year.¹⁸ In patients who initiated ICS therapy (n=1319), the odds ratio (OR) for achieving asthma control with HFA-BDP was 1.30 (95% CI, 1.02-1.65; number needed to treat, 12) relative to HFA-/CFC-FP. In patients who stepped up therapy (n=250), there was no difference in asthma control with HFA-BDP compared to HFA-/CFC-FP. Data such as these led van den Berge et al¹⁹ recently to conclude that “[n]ewly developed devices enable drugs to target the small airways, and this may have implications for treatment of patients with asthma, particularly those not responding to large-particle inhaled corticosteroids or those with uncontrollable asthma.” Further investigation is ongoing.

From a safety perspective, higher serum levels of BDP have been observed following treatment with HFA-BDP 200 µg, 400 µg, or 800 µg daily compared to that with CFC-BDP 800 µg daily for 2 weeks, although there was no difference in suppression of the hypothalamus-pituitary-adrenal (HPA) axis between the 800 µg doses.²⁰ In other studies, no significant differences in morning plasma cortisol were found with HFA-BDP compared to CFC-FP over 6 weeks,²¹ while the urine free-cortisol level was found to be significantly decreased over 12 weeks with CFC-FP 88 µg twice daily compared to baseline ($P=.0103$) but not with HFA-ciclesonide 160 µg daily.²² Similarly, the effect on the HPA axis was observed to be significantly less with HFA-

ciclesonide compared to CFC-budesonide ($P<.001$).¹⁷ Oropharyngeal candidiasis and dysphonia appear to be less common with an HFA ICS than with a CFC ICS.¹¹

The impact of HFA ICS on growth in children is under investigation. The results of 1 open-label study showed no significant differences in growth over 1 year with CFC-BDP 200 µg to 400 µg daily compared to BDP at half the daily dose.²³ However, a meta-analysis by Sharek and Bergman found that BDP in doses of 328 µg to 400 µg daily suppresses growth when given for a minimum of 3 months.²⁴ These results are in agreement with a recent study funded by the National Heart, Lung, and Blood Institute, which found 1.1 cm less linear growth than placebo in children treated with HFA-BDP 40 µg twice daily for 44 weeks.²⁵ Another study involving ciclesonide 40 µg and 160 µg once daily found no effect on linear growth over 1 year compared to placebo in children 5 to 8.5 years of age; at the same time, there was no difference in efficacy between the ciclesonide and placebo groups.²⁶ However, since the approved dose of ciclesonide is 80 µg to 320 µg twice daily,²⁷ the 40-µg and 160-µg once-daily doses used in this study may not provide a full estimate of the effect of ciclesonide on growth.

Role of long-acting inhaled β-agonists

The role of LABAs in the treatment of patients with asthma has been a subject of ongoing discussion since salmeterol became available in 1994. Much of this discussion has been fueled by the results of the Serevent Nationwide Surveillance (SNS) study in 1993²⁸ and the Salmeterol Multicenter Asthma Research Trial (SMART) in 2006.²⁹ Both trials demonstrated a slightly greater but statistically insignificant ($P>.05$) risk of respiratory-related death and asthma-related death in patients treated with salmeterol compared to albuterol²⁸ and placebo.²⁹ For asthma-related death, for example, the relative risk of death due to salmeterol was 3.0 in SNS and 4.37 in SMART. Based on these and other data, the NAEPP EPR3 advised that “the beneficial effects of LABA in combination therapy for the great majority of patients who require more therapy than low-dose ICS alone to control asthma (ie, require step 3 care or higher) should be weighed against the increased risk of severe exacerbations, although uncommon, associated with the daily use of LABAs...”²² This recommendation, which was consistent with the then-approved indications for salmeterol³⁰ and formoterol,³¹ makes it clear that LABAs should not be used as initial therapy and should be added only to anti-inflammatory controller therapy, typically an ICS.²

However, inappropriate use of a LABA is common in patients who have not previously taken an ICS and/or who have mild persistent asthma, as is shown in several retrospective analyses of insurance claims databases.³²⁻³⁴ Friedman et al found that among a study population of adults and children aged ≥12 years (N=87,459), more

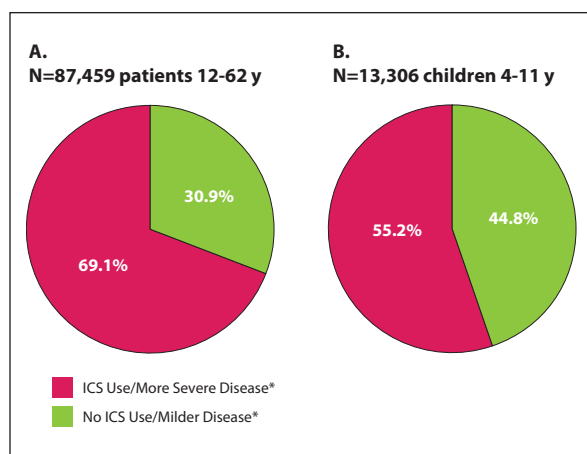
than two-thirds (69.1%, n=60,453) of individuals who were prescribed the FP/salmeterol combination had neither received ICS therapy before their first claim for FP/salmeterol nor had evidence of moderate or severe persistent asthma (FIGURE 2A).³² A subsequent analysis by the same investigators in children aged 4 to 11 years (N=13,306) showed that the FP/salmeterol combination was used as initial therapy in more than half (55.2%, n=7351) of children with mild to moderate persistent asthma (FIGURE 2B).³³ A more recent analysis found that 65.6% (5523/8424) of patients diagnosed with mild persistent asthma were being treated with an ICS/LABA combination rather than ICS monotherapy.³⁴

In 2008, the FDA conducted its own meta-analysis of 110 studies involving 60,954 patients with asthma aged ≥4 years who were treated with a LABA alone or in combination with an ICS.³⁵ The results showed that LABAs were associated with an increased risk of asthma-related events versus non-LABA treatment (risk difference 2.8/1000 treated patients; 95% CI, 1.11-4.49), as measured by the asthma composite end point, which included asthma-related death, asthma-related intubation, and asthma-related hospitalization. The results were driven primarily by asthma-related hospitalizations.

Coupled with the results of the SNS and SMART trials, this meta-analysis led the FDA to conclude that there is “an increased risk for severe exacerbation of asthma symptoms, leading to hospitalizations in pediatric and adult patients as well as death in some patients using LABAs for the treatment of asthma....”³⁶ As a result, the FDA required labeling changes for LABAs in the treatment of asthma (TABLE 2) but not chronic obstructive pulmonary disease,³⁷ as well as the implementation of a risk evaluation and mitigation strategy (REMS).³⁶ The FDA’s actions support the NAEPP EPR3 evidence-based recommendations that a LABA should not be used alone without concomitant use of an asthma controller medication such as an ICS in patients of all ages with asthma.^{2,37}

However, other labeling changes required by the FDA are not consistent with the recommendations adopted by the NAEPP EPR3, which has led many asthma experts, including the chair of the NAEPP EPR3, William W. Busse, MD, to raise concerns over the FDA’s actions.³⁸ For example, the new LABA labeling indicates that LABAs should not be used in patients whose asthma is adequately controlled on low-dose or, importantly, medium-dose ICS. The new labeling and NAEPP EPR3 recommendations are in agreement with respect to patients adequately controlled on low-dose but not medium-dose ICS. The NAEPP EPR3 recommends that increasing ICS monotherapy from a low to a medium dose should be given equal weight to the option of adding a LABA to a low-dose ICS.² In children 6 to 17 years

FIGURE 2 Use of LABA/ICS as initial therapy*^{33,34}



*During the 365 days prior to the first claim for fluticasone/salmeterol. ICS, inhaled corticosteroid; LABA, long-acting β-agonist.

of age with uncontrolled asthma, recent evidence from the Best Add-on Therapy Giving Effective Responses (BADGER) trial supports the superior efficacy of adding a LABA to a low-dose ICS instead of increasing the ICS to a medium dose.³⁹

Another point of disagreement concerns the FDA’s recommendation to use LABAs in combination with a long-term controller such as an ICS. This recommendation suggests that all long-term controllers are of similar benefit when used in combination with a LABA; however, the NAEPP EPR3 found the use of a LABA in combination with an ICS to be superior to a LABA in combination with a leukotriene receptor antagonist (LTRA) in patients ≥12 years of age.² Here again, the BADGER trial showed that in children 6 to 17 years of age with uncontrolled asthma, the addition of a LABA to a low-dose ICS was superior to adding an LTRA to a low-dose ICS.³⁹ The reader is referred to the recent editorial by Lemanske and Busse³⁸ for further discussion comparing the FDA labeling changes with the NAEPP EPR3 recommendations.

Let’s return to our 2 cases and see what changes should be made to the treatment plans to regain asthma control.

Case 1 (7-year-old female)

- Switch anti-inflammatory therapy from montelukast to a low-dose ICS
- Add a LABA (in a single device with the ICS)
 - Initiating monotherapy with a medium-dose ICS is an equally acceptable alternative
 - Initiating a low-dose ICS in combination with an LTRA would be a less preferred alternative
 - Evaluate allergy status

TABLE 2 New labeling for long-acting β -agonists (LABAs) as recommended by the US Food and Drug Administration³⁷

<ul style="list-style-type: none"> • Use of a LABA alone without use of a long-term asthma control medication, such as an inhaled corticosteroid (ICS), is contraindicated (absolutely advised against) in the treatment of asthma
<ul style="list-style-type: none"> • LABAs should not be used in patients whose asthma is adequately controlled on low- or medium-dose ICSs
<ul style="list-style-type: none"> • LABAs should be used as additional therapy only for patients with asthma who are currently taking but are not adequately controlled on a long-term asthma control medication, such as an ICS
<ul style="list-style-type: none"> • Once asthma control is achieved and maintained, patients should be assessed at regular intervals and step-down therapy should begin (eg, discontinue LABA), if possible, without loss of asthma control, and the patient should continue to be treated with a long-term asthma control medication, such as an ICS
<ul style="list-style-type: none"> • Pediatric and adolescent patients who require the addition of a LABA to an ICS should use a combination product containing both an ICS and a LABA to ensure adherence with both medications.

- Continue SABA prn
- Monitor symptom improvement
- Follow up for reevaluation in 2 to 6 weeks

Case 2 (25-year-old female)

- Increase the ICS to a medium dose
 - Adding a LABA to a low-dose ICS in a single device is an equally acceptable alternative
- Evaluate allergy status, especially molds
- Continue SABA prn
- Monitor symptom improvement
- Follow up for reevaluation in 2 to 6 weeks

While there is a clear need for follow-up visits for reevaluation, the focus of an office visit should be both maintenance of asthma control and treatment of asthma exacerbations rather than solely treatment of asthma exacerbations. Such asthma maintenance visits are consistent with the core concepts of the patient-centered medical home as well as the management approach for patients with other chronic diseases such as hypertension and type 2 diabetes mellitus. In addition, asthma maintenance visits provide an ongoing opportunity to reinforce patient self-management.

Patient self-management

As with other chronic diseases, the willingness and ability of patients with asthma to self-manage their disease are critical for optimal long-term outcomes. The benefits of patient self-management for asthma include an increase in the number of symptom-free days,⁴⁰ a decrease in work/school absenteeism,^{40,41} improvement in health status and quality of life,^{41,42} a decrease in urgent care visits and hospitalizations,⁴³ and a decrease in asthma-related health care costs.^{41,42}

Given the numerous potential benefits of good patient self-management, it is important to understand that a positive attitude, knowledge, and self-efficacy are important determinants of disease self-management.⁴⁴

Helping patients recognize and believe that they can improve their exercise stamina, minimize the impact of their disease on daily activities, and improve their sleep with appropriate use of currently available treatments should be a major focus. Good physician-patient communication is required, as is a good physician-patient relationship. This relationship should be based on shared goals—goals that are determined by the patient with assistance from the physician—and reinforcement and support from the physician as the patient achieves those goals.⁴⁵ Fully achieving these may be difficult owing to time and resource constraints in the typical primary care setting. However, one barrier where significant improvement may be possible is in physician-patient communication. A review of local, national, and multinational surveys completed by asthma patients found that physicians may engage in poor or unstructured communication with their asthma patients.⁴⁶ One approach that can better structure communication during the office visit and provide patients with critical information to improve self-management is the development of a WAAP.

Written asthma action plan

The development of a WAAP is an opportunity for the physician and the patient to discuss and agree on a treatment plan that the patient can follow at home. A WAAP is recommended especially for patients who have moderate or severe persistent asthma, a history of severe exacerbations, or poorly controlled asthma.² Involving the patient and customizing the plan to his or her needs, functional abilities, language, culture, age, health literacy, and numeracy (ability to understand and reason with numbers) can lead to improved utilization of the WAAP by the patient⁴⁷ and improved long-term adherence and patient outcomes.^{48,49} It is also important to keep in mind that the WAAP is dynamic and should change in response to the patient's needs and self-management experience. Doing so has been shown to be integral to patient ownership and use of the plan.⁴⁷

WAAPs include 2 important elements (FIGURE 3).² The first is a road map for daily treatment and monitoring. Inclusion of this information is essential to promote maintenance of asthma control. Details of the road map include what medicine(s) to take, with both generic and trade names listed, as well as why, how, how much, and when to take them. Actions to take to control environmental factors that worsen the patient's asthma should also be included. Instructions for monitoring asthma-related symptoms should be provided, as well as the expected results of treatment.

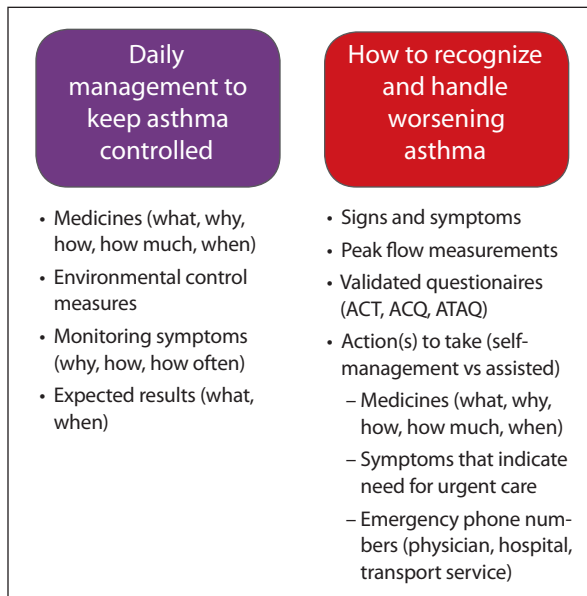
The second element of a WAAP details how to recognize and handle worsening asthma.² Whether the WAAP should be symptom based or peak-flow based is under investigation, as clinical trials have shown each plan to be superior to the other,^{49,50} suggesting that individualization based on patient characteristics is essential. In either case, signs and symptoms of worsening asthma should be listed, including peak expiratory flow measurements, if used. The names of the medicines to take in response to worsening asthma control, as well as how to take them and how much to take, should be included in this element of the action plan. It is also essential that signs and symptoms indicating the need for urgent medical attention be clearly differentiated. Emergency telephone numbers, for example, for the patient's physician, the nearest hospital, and a transport service, should also be included. The concomitant use of validated questionnaires, such as the ACT, C-ACT, ACQ, or ATAQ, may also help patients recognize worsening asthma control.

Returning to the 2 case studies, there are several self-management issues to be addressed. These issues must, of course, be individualized, and in the case of the 7-year-old patient, must include the parents.

Case 1 and Case 2

- Educate the patient (and parents) about the goals of treatment and the importance of anti-inflammatory medication
- Stress that there is room for symptom improvement, as well as the importance of not simply accepting worsening symptoms or a diminished quality of life and daily functioning
- Review inhaler technique
- Use an in-check dial to measure correct inspiratory flow rate
- Review peak flow meter technique
- Review when and how to use their medications, including a SABA
- Discuss environmental control measures (especially for the older patient)
- Assess adherence to the treatment plan
- Collaboratively develop a WAAP that includes both a daily road map for treatment and monitoring and a plan to recognize and handle worsening symptoms

FIGURE 3 Elements of a written asthma action plan (WAAP) as recommended by the National Asthma Education and Prevention Program (NAEPP) Expert Panel Report 3 (EP3)²



ACT, Asthma Control Test; C-ACT, Childhood Asthma Control Test; ACQ, Asthma Control Questionnaire; ATAQ, Asthma Therapy Assessment Questionnaire.

- Review what to do with worsening lung function, which is especially important if a LABA is added to the treatment plan

Summary

There has been little improvement over the past decade in morbidity and limitations on activity for patients with asthma, and there appears to be considerable opportunity for improved patient self-management. Inflammation is the central problem in asthma and occurs in both the large and small airways; however, there seems to be a lack of understanding among patients about the role of inflammation in asthma and the need for daily controller medication to address this issue. Patients are often prescribed a LABA/ICS combination as initial therapy for mild persistent asthma, yet the NAEPP EPR3 clearly indicates that an ICS is first-line therapy. If asthma control is not achieved, options for step-up therapy include either an increased dose of ICS or a LABA/ICS combination. To address safety concerns, the FDA has required labeling changes for LABAs, as well as a risk evaluation and mitigation strategy; however, the labeling changes have been questioned as being inconsistent with evidence-based recommendations made by the NAEPP EPR3 in 2007. While the role of LABAs is under debate, there is agreement that use of a LABA without a long-term controller

for mild persistent asthma is contraindicated. Efforts to improve patient self-management with such tools as a written asthma action plan should occur at every asthma maintenance visit. ■

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