Asthma

Justin Rucci, MD, Pnina Weiss, MD

To know even one life has breathed easier because you have lived. This is to have succeeded.
—Ralph Waldo Emerson

Learning Objectives:
1. Describe the pathophysiology, triggers and risk factors for asthma
2. Classify asthma severity and assess asthma control according to national guidelines
3. Propose an appropriate treatment plan based on disease severity
4. Model asthma-related patient counseling and develop an asthma action plan

Primary References:

CASE ONE:

Ivan Tobreath is a 12-year-old boy who presents to clinic for a school physical. He has had asthma since he was two years old, but no other significant past medical history. He has never been hospitalized, but has had two Emergency Department visits in the last six months. Each time, he improved after several nebulizer treatments and was sent home with a course of prednisone. His mother reports that his asthma is “well-controlled” with an albuterol metered-dose-inhaler (MDI) without spacer, which he uses once or twice a month. Upon directly questioning Ivan, he reports that he actually uses his MDI daily before exercise, and 3-4 times a week for shortness of breath. He wakes up in the middle of the night 3-4 times a month because of “chest tightness.” On physical exam, his vital signs are within normal limits and he is in no acute distress. Lung examination reveals occasional expiratory wheezes with forced exhalation. Peak flow is 310 L/min (360 L/min predicted).

1. How would you classify the severity of his asthma?

The National Asthma Education and Prevention Program (NAEPP) first published asthma severity classification guidelines in 1991 with the goal of using severity to choose the best initial treatment and follow-up plan, guide patient and family education, and create standard definitions for research purposes. The classification has undergone multiple revisions, most recently in 2007.

Severity of asthma is defined as the intrinsic intensity of the disease process. It is most easily measured in untreated patients. This is distinct from control, which is defined as the degree to which manifestations of asthma are minimized and the goals of therapy are met.

Severity and control are assessed in two domains: impairment and risk. Impairment refers to the frequency and intensity of symptoms, and limitations in activity and lung function. Risk refers to the likelihood of asthma exacerbations or progressive loss of pulmonary function over time. According to the 2007 NAEPP guidelines, Ivan would be considered to have at least mild persistent asthma since he has symptoms more than twice per week but not daily, nighttime symptoms greater than twice a month, a peak flow in the 80-100% range (86% if calculated based on a height of 59”) and at least two exacerbations a year. Though Ivan uses albuterol before exercise daily, he does not currently meet criteria for moderate persistent asthma. It is the frequency of bronchodilator use for relief of symptoms that is used to
To use an MDI: It is also helpful to stress that this must be differentiated from the frequency of bronchodilator use to prevent exercise-induced asthma. Moderators should review the classification of asthma in patients ≥12 years as appears in Figure 1 of the Wechsler article and highlight that severity is assigned to the most severe category in which any feature occurs; the classification for children <12 differs only slightly as outlined in Figure 11 the 2007 NAEPP summary report.

2. How would you manage Ivan’s asthma now that you know its severity? Does he require an inhaled corticosteroid?

At this point, Ivan would most likely benefit from a maintenance therapy. According to 2007 NAEPP Guidelines, the treatment of choice would be low dose inhaled steroids (ICS). Alternative therapy with leukotriene receptor antagonists (LTRA) could be considered. Cromolyn, nedocromil, and theophylline are also listed as alternative therapies, however, their use and availability are limited.

ICS are available in MDI, dry-powder inhalers (DPI), and nebulized forms. MDIs and DPIs are generally easier to use than nebulizers; they are portable, do not require electricity, and the entire treatment is shorter (relative to a 5-minute nebulized treatment). It may also be helpful to point out to patients requesting a nebulizer that there are potential ocular side effects (i.e., cataracts) associated with nebulized ICS due to the higher local dose delivered to the eyes. Children should rinse their mouths out after treatments with ICS (through any delivery system) to avoid local side effects in the oropharynx (e.g., thrush, sore throat) as well as systemic side effects from any ingested steroid.

3. What specific patient education would you provide? How would you describe the proper use of an MDI? A peak flow meter?

Consider having learners role-play the conversation that a practitioner might have with Ivan and his mother.

As with any disease, education is just as important as the medications prescribed. For optimal asthma management, the patient and family must understand the disease, its impact and harm if not treated adequately, and rationale behind treatment. The use of patient educational materials (e.g., hand-outs, models of respiratory system, sample inhalers) can be useful in helping patients understand the disease. As always, education should be tailored appropriately to the patient and family and will likely require repetition over many visits.

For Ivan, a 12-year-old with a long history of asthma, it would be helpful to review the basic pathophysiology of asthma, with a focus on the idea that bronchospasm/airway hyperresponsiveness and chronic inflammation both play roles in the disease. This may help him to understand his new regimen of two inhalers: rescue albuterol when needed to manage bronchospasm and maintenance ICS to control inflammation.

Education regarding factors that may precipitate or aggravate symptoms should be provided, both to help avoid exposure and to identify the triggers to which he is most susceptible. Common triggers include environmental allergens (mold, house-dust mite, cockroach, pollens), viral infections (RSV and rhinovirus), tobacco smoke, exercise, irritants (strong odors, dusts, aerosolized chemicals), and changes in weather or exposure to cold air.

It is also important to stress the proper technique to use an inhaler and ensure that MDIs are used with a spacer.

To use an MDI:
1. Remove cap, shake inhaler.
2. Attach inhaler to spacer/mask.
3. Breathe out fully.
4. After the next breath is initiated, press down to activate the inhaler
   a. For older children, they should then inspire deeply and hold that breath for 5-10 seconds.
   b. For younger children using a spacer with mask, keep the mask securely attached to their face and allow them to breathe approximately 10 breaths.
   c. Many spacers are equipped with a whistling mechanism that sounds if the child is inhaling too quickly which results in inadequate medication delivery.
5. If a second puff is needed, repeat with the same technique (no need to wait between puffs with new MDIs).
6. Replace cap and store medicine in a cool, dry place. It is also important to keep the spacer clean to ensure proper flow of medication and prevent inhalation of foreign debris.
7. Rinse mouth (recommended for steroids, not bronchodilators).

If appropriate, the family should learn how to use a peak flow meter. Peak flow monitoring may detect early changes in symptom severity and guide changes to therapy when used as part of an asthma action plan.

To use a peak flow meter:
1. Be sure that the patient is standing, not sitting.
2. Reset meter to zero or lowest number on peak flow.
3. Take as deep of a breath as possible and secure lips firmly around mouthpiece, creating a tight seal.
4. Breathe out forcefully; think “fast hard blast” rather than slow controlled exhalation.
5. Repeat entire process three times and record the highest number on peak flow log.
6. Compare result with peak flow recommendations on the asthma action plan.

At this point, moderators can have learners compose an asthma action plan (see Resources).

CASE continued:

You discuss your plan to start maintenance therapy to obtain better control of Ivan’s asthma. Immediately upon hearing “steroid,” Ivan’s mother becomes worried about his growth.

4. Is her concern warranted? What impact do inhaled corticosteroids have on growth?

Growth suppression is a concern with oral steroids, though the use of chronic systemic steroids is rarely needed to control childhood asthma. The effect of ICS on growth has been controversial. Short-term studies of first generation ICS (beclomethasone) revealed subtle differences in linear growth. Studies using second-generation ICS (fluticasone and budesonide) revealed mild growth suppression (on the order of 1 cm of less) during the first year of therapy, however the effect resolved after four years. The use of high dose ICS during exacerbations has been associated with slower growth rates in a dose dependent manner. Studies on the impact on predicted adult height have had mixed results.

As mentioned above, proper administration of ICS (e.g., use of spacer, rinsing mouth) can reduce systemic absorption. Providers should continue to follow growth parameters closely in children using ICS and weigh the risks and benefits with the patients and families on an ongoing basis.

CASE continued:

Ivan returns to see you in 6 weeks and reports that he feels much better. He used his albuterol MDI, now with spacer, only once last week. He denies nighttime symptoms and even notices that he can exercise more. His peak flow is 360 L/min.

5. Would you downgrade this patient's asthma severity? What tools can longitudinally assess asthma control in patients already diagnosed with the disease? Would you consider stepping down his therapy?

The NAEPP asthma severity categories are based on symptoms prior to initiating therapy, and therefore Ivan’s severity should not be downgraded. Unfortunately, once control is achieved with appropriate therapy it is not uncommon for patients or families to discontinue controller medications and subsequently return with an acute exacerbation. It is critical to point out that asthma is a chronic disease and that the reduction in symptoms is likely due to the addition of ICS.

At this time, it is necessary to assess Ivan’s symptom control. This is done through a combination of subjective questioning related to symptoms and objective parameters of lung function in appropriately-aged patients (e.g., peak flow, spirometry, exhaled nitric oxide). **Moderators should review the classification of control as appears in Figures 2-4 of the Wechsler article.** Of note, there are several
valldated patient-reported composite asthma scoring symptoms that can be utilized, which allow the
degree of asthma control to be compared across encounters. Some of the most commonly used are the
Asthma Control Questionnaire (ACQ for ages 6-17), Asthma Control Test (ACT for ages 12 and older) and
the Childhood Asthma Control Test (C-ACT for children ages 4-11) (See Resources). For children under
age 4 suspected of having asthma, the test for respiratory and asthma control in kids (TRACK) is available.
Importantly these tools strive to have the patient answer questions related to their symptoms, as it has
been reported that children may assess their asthma control to be significantly worse than their parents
do.

The 2007 NAEPP guidelines recommend a minimum of 3 months of well-controlled asthma before
considering stepping down therapy, and some experts wait at least 6 months. There may be seasonal
variation to a child’s asthma (due to allergies or upper respiratory infections). In general, asthma
exacerbations are more frequent in the fall and winter so summer may be a good time to consider a
honeymoon off medications or to step down therapy. Keep in mind the converse may be true if a patient’s
asthma is regularly triggered by outdoor allergens such as tree or grass pollens.

6. What interventions may help maintain adequate control of the patient’s symptoms?

Unfortunately, numerous studies have shown that asthma control in the pediatric population may not be
adequate despite national guidelines for management. While health care providers cannot control all
factors related to a patient’s asthma management, steps can be taken to improve asthma control.

Ensuring appropriate follow up is an important component of management. National guidelines
recommend that children with persistent asthma have at least 2 preventive asthma visits (PAV) per year.
Despite this recommendation follow-up is often under-utilized, with one study demonstrating that among
urban children with persistent asthma as many as 75% had no PAV. One approach is to have a patient
with poor control return in 4-6 week intervals until asthma symptoms have improved and subsequently
to have frequent, brief visits (e.g., every 3 to 6 months). These visits can be used to re-assess symptom
control, ensure understanding of treatment regimens, evaluate for any modifiable exposure to triggers,
confirm appropriate MDI use by patients, reinforce educational topics discussed previously and assess for
changes in a family’s social or economic situation that may contribute to suboptimal control. During any
visit in the fall or winter months, the provider should verify that the patient and family have been offered
or have received the influenza vaccine. Other novel strategies have been implemented in hopes of
improving asthma management, such as school-based asthma management programs and online patient
reminders related to asthma medications and self-care. While these have had some promising initial
results, larger studies are needed before they are initiated on a broader scale.

CASE continued:

| Two months later, Ivan returns after yet another visit to the Emergency Department. |

7. Should Ivan’s medications be stepped up? If so, what medications should be used

Before increasing his medications, it is important to determine any potential modifiable reasons for the
treatment failure. The most common issues which can affect a previously well-managed patient are
easily remembered by the mnemonic ICE. Inhaler technique should be reviewed, including the use of a
spacer and ensuring that an MDI is not empty. Compliance with daily controller medications should be
evaluated. Environmental changes, such as seasonal allergies or a new pet, may also predispose the
patient to an exacerbation. In addition, the provider should assess the patient for any concomitant upper
airway illness, comorbidities, or alternative diagnosis.

Once you determine that Ivan has been using his medications appropriately, it would be appropriate to
step up his medications to gain better control. The 2007 NAEPP guidelines list the preferred next line of
treatment as either medium dose inhaled corticosteroids or combination therapy with low-dose ICS and
a long-acting beta agonist (LABA). Alternative treatment includes consideration of the combination of
low-dose ICS with a LTRA.

There have been safety concerns about the use of LABAs in patients with asthma. In the 2006 Salmeterol
Multicenter Asthma Research Trial (SMART), a small but statistically significant increase in asthama-
related death was found in the group assigned to salmeterol compared to placebo (in addition to “usual asthma care”) with a sub-group analysis demonstrating the greatest risk in African Americans. However, in 2016, a randomized controlled trial of 6208 pediatric patients with asthma mandated by the Food and Drug Administration (FDA) demonstrated that there was no increase in the risk of serious asthma-related events in patients using a fluticasone-salmeterol combination inhaler when compared to fluticasone alone, suggesting the LABA+ICS strategy is likely safe in pediatric patients. After conducting a meta-analysis that included this study and three others with a similar design (a total of 41,297 patients), the FDA found that the use of LABA+ICS inhalers does not result in significantly more asthma-related deaths than ICS alone. Therefore, the FDA has removed it’s “Boxed Warning” about asthma-related deaths from drug labels of LABA+ICS inhalers.

LABA monotherapy should not be used in pediatric asthma since significant safety concerns remain. Several potential mechanisms have been proposed. First, that LABAs have a direct effect on bronchial smooth muscle and increase bronchoconstriction in response to a specific stimulus. Secondly, that LABAs can mask worsening inflammation, which leads to a delay in seeking medical attention or to catastrophic airway obstruction that is less responsive to short acting beta agonists. Polymorphisms in the beta2-adrenergic receptor gene, which may increase susceptibility to the effects of the beta2-agonists, have been investigated, but results have been inconclusive.

Alternatively, medium dose ICS monotherapy can be considered. A recent meta-analysis demonstrated that regular use of ICS is unlikely to increase the risk of pneumonia or other respiratory infections in children with asthma. However, there may be side effects associated with use of moderate dose ICS. In particular, one study showed that higher doses of ICS may be associated with greater growth suppression than the combination of lower doses of ICS with LABA.

Given the current data, there is not a uniform solution for every patient requiring this level of therapy. It is therefore appropriate to incorporate the family and patient in decision making to achieve the optimal treatment plan.

8. Which patients should be referred to an asthma specialist?

The 2007 NAEPP recommendations for referral to an asthma specialist include:

- Atypical signs and symptoms
- Difficulty achieving or maintaining asthma control
- The need for >2 bursts of oral systemic corticosteroids in 1 year
- An exacerbation requiring hospitalization
- The use of combination therapy of ICS plus LABA or LTRA to maintain control (or medium dose ICS alone for children 0-4 years of age)
- Consideration of immunotherapy or omalizumab
- Additional testing indicated

CASE continued:

Ivan’s asthma control improves dramatically over the next many months. You have read that the overall prevalence of pediatric asthma has plateaued since 1980, but this seems hard to believe given how frequently you care for children with asthma exacerbations.

9. Describe the factors that lead to disparities in asthma outcomes.

Unfortunately, there are still significant disparities in asthma outcomes associated with race, ethnicity, and socioeconomic status; these include morbidity, mortality, and rates of emergency room visits and hospitalizations due to asthma. A multitude of social and structural factors lead to these disparities, including limited access to primary and subspecialty care, increased exposure to indoor allergens and other environmental triggers, poorer health literacy, implicit bias (with minority children less likely to be prescribed a controller mediation when indicated as compared to their white peers), and health care policy. No single intervention is likely to address all these disparities, and to date the most effective strategies have been tailored to local environments/issues, and have tackled as many “levels of influence” - patient/family, provider, microsystem, organization, community, and policy - as possible.
For example, healthcare organizations can partner with schools and community organizations to reach children and families in their environments rather than only in clinical spaces. Moderators wishing to expand this part of the discussion can direct Learners to the 2017 article by Volerman and colleagues, as well as the separate module on Poverty & Social Determinants of Health within the curriculum.

Additional References:

Resources:
1. Asthma information for providers, including PDA resources and asthma action plans (English and Spanish). http://www.nhlbi.nih.gov/health/prof/lung/index.htm
2. Asthma information for patients and families. 

**Acknowledgment:**
The current authors would like to thank Drs. Nick Pietris and Alia Bazzy-Asaad for their work on a previous version of this chapter.