AN INTRODUCTION TO ASTHMA

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Asthma is the most common chronic condition in childhood, affecting an estimated 5 million children in the United States. More children miss school for asthma than for any other chronic condition. The prevalence of asthma has steadily risen over the past 25 years for reasons that are not clear.

Asthma is characterized by inflammation of the airways. This inflammation consists of mast cells, lymphocytes, eosinophils and, in severe cases, neutrophils. Inflammation is always present in the airways, even at times when patients are clinically well. Over time, the airways can develop structural changes including collagen deposition beneath the epithelium, and thickening of the basement membrane and smooth muscle, a process known as “remodeling.”

Identification of patients

Patients with asthma are usually identified after a careful history. Typically, parents will complain of recurrent cough (especially at night), wheeze or shortness of breath, provoked by a variety of triggers, including exercise, weather changes, pollens, colds, smoke, strong smells, animals, cold air, and humidity. The physical examination may be normal, or may show hyperinflation of the chest, wheeze, prolongation of exhalation, or other signs of allergy, like eczema and nasal inflammation. If a child has digital clubbing, nasal polyps, abdominal bloating, or is failing to thrive, the diagnosis of cystic fibrosis should be considered, and the child referred for a sweat test. Spirometry (pulmonary function testing) is useful to detect the presence and reversibility of airflow obstruction. While the test is most frequently normal, the presence of obstruction would automatically place the child in a moderate persistent category of asthma (definition is below). Also, the obstruction should be at least partially reversible (at least a 12% improvement in FEV₁) either by a bronchodilator, or by a course of oral corticosteroids, otherwise, an alternative diagnosis should be considered. Thus, if obstruction is present, it is important to repeat the spirometry after bronchodilator and steroid therapy to document the response.

It is important to note that in some patients, the predominant symptom is cough, with a prominent nocturnal component. A lack of wheeze history does not necessarily rule out asthma.

The management of asthma consists of two components: prevention and rescue.

Prevention

Prevention of asthma exacerbations is accomplished by taking steps on a daily basis to minimize airway inflammation. It is important to identify and avoid triggers, as these serve to increase the
airways inflammation and set off asthma attacks. Allergy testing is immensely helpful; most children with asthma have allergies, and identification of allergens is useful to guide parents in knowing what changes they need to make in their child’s environment to reduce exposure. While allergy skin testing can be done at any age, useful information is usually obtained after the age of about three. Babies with eczema may have food allergy, and should be tested in infancy. Avoidance of environmental tobacco smoke is of paramount importance, and patients with asthma should never take up smoking! Patients with asthma should also take appropriate precautions on days with high levels of atmospheric ozone or other pollutants.

In children, viral respiratory infections are associated with 80% of asthma exacerbations requiring urgent visits or hospitalizations. Influenza vaccination is very important in children with asthma, as they are at high risk for complications from the flu. Asthmatics should not receive the live virus nasal vaccination, as increased wheezing was noted in asthma patients who had received this vaccine in the clinical trials. Unless egg or chicken allergy is present, killed virus flu vaccine is not associated with more complications in asthma patients than is placebo. Careful consideration should be given to frequent handwashing, either with soap and water or with waterless soap, and to avoid touching one’s hands to the face unnecessarily or when not freshly washed. Most respiratory viruses are contracted after contact with infected secretions on surfaces.

If patients are not responding to asthma therapy, consideration should be given to look for “internal” triggers such as sinusitis and gastroesophageal reflux. Referral to a specialist (anyone who specializes in asthma, usually an allergist or pulmonologist, see the appendix) should be considered also, to make sure that the patient does not have another disease.

In addition to trigger avoidance, medications are used on a daily basis to prevent exacerbations. All maintenance regimens should consist of at least one anti-inflammatory agent. Some patients also require long-acting bronchodilators, but these should always be given in conjunction with an anti-inflammatory medication. The choice and dose of anti-inflammatory medication is predicated on the severity of the child’s asthma. The NIH-NAEPP (ie: the US national) asthma guidelines recognize four levels of asthma severity; these will be discussed below, along with the pharmacologic approach to each level of severity.

There are a number of classes of prevention (controller) medicines available. These are:

1. Corticosteroids: available for inhaled and systemic administration. Inhaled corticosteroids are the mainstay of asthma controller therapy, while systemic steroids are primarily used for management of exacerbations (although some patients with severe asthma require small doses of systemic steroids on an ongoing basis to control their asthma). These drugs reduce inflammation, prevent exacerbations, and may reduce the rate at which permanent structural changes occur in the airways. The side effects of systemic steroids are well known, but generally not a problem with the use of short courses for rescue. The risk of such side effects from inhaled steroids, while not zero, is generally much lower than that from oral steroids. There is a risk of thrush, which can be virtually eliminated with rinsing the mouth after the use of the medication. Occasionally, hoarseness can develop, which can be bothersome to choristers. To reduce the risk of
oral complications, it is important to train the patient in the appropriate use of the device, and to use spacers if a pressurized metered dose inhaler is used. There has been some question raised in the literature about reduced linear growth in children on inhaled steroids; recent long-term studies, though, have been reassuring. The risk of adrenal suppression on inhaled steroids, while not zero, is less than the risk of a bad traffic accident while driving on the Alabama interstates in the rain! Side effects can be minimized by using the dose of inhaled steroids necessary to control the disease, then backing down to a lower dose once control is achieved.

2. Leukotriene antagonists: available for oral administration. These agents block the leukotrienes, important mediators of inflammation in asthma. The effects of these agents vary among patients; some respond dramatically, some have some response, and some do not respond at all. While leukotrienes are important mediators in asthma, they are not the only ones; and variation in response may depend in part on how much the leukotrienes are playing a role in an individual person. Side effects are generally minimal.

3. Long-acting bronchodilators: beta agonists whose airway effects last about 12 hours. The onset of action is slower than rapid acting beta agonists, so they are for prevention, not rescue. Deaths have been reported in patients using these drugs as monotherapy; hence, they must always be used in conjunction with an anti-inflammatory agent, preferably an inhaled steroid.

4. Cromones: these include cromolyn and nedocromil, drugs for inhalation. These drugs stabilize mast cells, and also have other complex actions which prevent the inflammation seen in asthma. These drugs are completely safe, but have to be given by inhalation 3-4 times a day at the outset, which reduces adherence.

5. Theophylline: this used to be the mainstay of asthma therapy. The mechanism of action is complex; the drug may have some anti-inflammatory as well as bronchodilator properties. The drug is a derivative of caffeine, and has a narrow window between therapeutic and toxic levels. Side effects include jitteriness, nausea, vomiting and in severe toxicity, seizures (which are ominous). Drug levels must be followed, which increases the cost of therapy of a drug that is otherwise inexpensive to buy. Therapeutic effect can be seen at lower levels than previously thought.

6. Anti IgE: commercially known as Xolair; a parenteral drug for selected individuals with severe asthma.

Rescue

Rescue medicines are given to children who are having asthma symptoms. Monitoring on the part of the patients and their parents can help to detect exacerbations early in the course, and can help them “nip them in the bud.” It is important to teach patients and parents the signs and symptoms of asthma exacerbations. The recognition of cough and increased respiratory rate as early signs of impending exacerbations can help parents nip these attacks in the bud, while the recognition of late signs, such as nasal flaring and chest wall retractions will guide them to seek prompt emergency care. Peak flow monitoring can be helpful, as well, to detect exacerbations early in their course and start treatment before the patient needs the emergency room or hospital. A complete discussion of peak flow monitoring is beyond the scope of this brief review; for more details, see the pediatric asthma CDROM distributed last spring by Alabama Medicaid.
Rescue medicines consist of the following:

1. **Rapid acting bronchodilators**: these are beta agonists; their onset of action is rapid, and result in bronchodilation, or opening of the airways. There are numerous agents on the market; inhaled beta agonists are far superior to their oral counterparts, as they provide more effective bronchodilation with fewer side effects. There is no role for these agents in prevention, with the exception of their use prior to PE/exercise. Beta agonists are given as frequently as every four hours at home, and even continuously in the hospital.

2. **Anticholinergics**: These are adjuncts to beta agonists in patients who are in emergency room settings.

3. **Corticosteroids**: patients with exacerbations of their asthma should in most cases receive a course of systemic steroids, to reduce inflammation and prevent recurrence. Occasionally, in patients with very mild exacerbations, a doubling of the dose of an inhaled steroid until symptoms resolve will be sufficient, but this is contraindicated in patients using combination products like Advair.

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**Appendix: chronic asthma management; classification of disease severity and selection of controller therapy**

Note: patients are classified at the highest level of severity for which they have any one criterion

**Mild intermittent**: Daytime symptoms no more than once a week, nighttime symptoms no more than twice a month, baseline lung function normal. Treatment: rapid-acting *inhaled* beta agonist as needed. If needing more than once a week for rescue, the patient needs anti-inflammatory therapy.

**Mild persistent**: Daytime symptoms more than once a week but not daily, nighttime symptoms more than twice a month, but not more than once a week, baseline lung function normal. Treatment: needs an anti-inflammatory. Low dose inhaled steroids are the most likely to make the patient well and are the official preferred therapy. Other options are leukotriene antagonists, a cromone or theophylline. Patients need also a rapid-acting *inhaled* beta agonist to use as needed. If needing more than once a week for rescue, the controller therapy needs to be rethought.

**Moderate persistent**: Daily daytime symptoms, or nighttime symptoms more than once a week, or baseline FEV1 60-80%, or history of a severe exacerbation (ER or hospital). Treatment: must include an inhaled steroid. Options are a medium dose, or a low dose coupled with a second controller agent, such as a leukotriene antagonist, long-acting bronchodilator, or theophylline. Also, the patient needs a rapid-acting *inhaled* beta agonist to use as needed; if needing more than one a week for rescue, rethink the controller therapy! Peak flow monitoring.

**Severe persistent**: Continual symptoms or FEV1 < 60%, or (in the opinion of the author) PICU admission. Treatment: high dose inhaled steroid, plus likely multiple other controllers. Rapid-acting *inhaled* beta-agonist to use as needed; if needing more than once a week for rescue, rethink controller therapy. Peak flow monitoring.
Appendix: specialist referral

Referral to a specialist should be considered when:

1. The patient has had a life-threatening exacerbation
2. The patient does not respond to asthma therapy
3. The patient’s symptoms are atypical, or you are unsure of the diagnosis
4. The patient has other complicating conditions, for example, congenital heart disease
5. The patient needs additional testing (for example, allergy testing should be seriously considered)
6. The patient is nonadherent and needs more education (specialists often employ patient educators)
7. The patient needs immunotherapy (which should always be carried out by a board-certified allergist)
8. The patient has severe persistent asthma (referral should be considered for patients with moderate persistent asthma, or any persistent asthma in children under three years of age)
9. The patient has received more than 2 bursts of systemic steroids over the course of a year
10. The patient is on high-dose inhaled steroids
11. You are uncomfortable managing the patient

For more information, see the asthma CDROM produced by Alabama Medicaid, or the links to the National Asthma Education and Prevention Program documents at the following website, http://www.nhlbi.nih.gov/health/prof/lung/index.htm#asthma