INTRODUCTION
A series of lectures on asthma and its management are given to third year doctor of pharmacy students in the fall semester. After discussions of the disease state, lectures on the therapeutic plan are presented, including long term management as well as emergency department (ED) and hospital treatment. Following these lectures, individual therapeutic agents are discussed, and asthma patient education is discussed in detail.

A brief note regarding teaching philosophy is appropriate at this point. Beyond sharing current literature in an organized fashion, the students observe a lot of enthusiasm as I discuss this topic. Because we are reviewing how to improve quality of life, and in some cases, save a life, I am naturally quite enthusiastic! In addition, my excitement for this subject is derived from being actively engaged in caring for asthmatics and conducting clinical research in management of this common condition. A major concern is that I insist in my students the desire to use this information in a variety of practice settings, including the community pharmacy, and not simply survive my examination. It is their choice to go out and make a difference for these patients and to be innovators, or to be passive, allowing patients to continue to suffer and have a diminished quality of life.

NIH GUIDELINES FOR LONG TERM MANAGEMENT
As discussed in earlier lectures, asthma is primarily an inflammatory condition. Based on this fact and the unfortunate reality of increased mortality from asthma, the National Institutes of Health (NIH) published in 1991 an Expert Panel Report entitled Guidelines for the Diagnosis and Management of Asthma(1). The following year a second landmark document, International Consensus Report on Diagnosis and Management of Asthma(1), was published by the NIH(2). These guidelines set the standard for long term and acute management of asthma. This paper will review the NIH guidelines for long term management and then cover other very recent literature to bring you right up to date on state of the art therapy.

The goals of therapy are as follows: (i) maintain normal activity levels (including exercise); (ii) maintain (near) “normal” pulmonary function rates; (iii) prevent chronic and troublesome symptoms (e.g., coughing or breathlessness in the night, in the early morning, or after exertion; (iv) prevent recurrent exacerbations of asthma; and (v) avoid adverse effects from asthma medications. To achieve these goals, the four major components of management are: (i) environmental control; (ii) objective monitoring with peak flow meters; (iii) patient education including a partnership between the patient and the health professional; (iv) and pharmacologic therapy.

Environmental Control
While a primary role of the pharmacist is not to assure environmental control, we can have a positive impact in this area. Encouraging patients to avoid or minimize exposure to asthma triggers is important. Whether the trigger is nonimmunologic (e.g., perfumes, cigarette smoke) or immunologic (e.g., household pets, ragweed), patients should be careful to keep exposure to a minimum. Consider household pets for a moment. Household pets are extremely important to many people. I have a basett hound, and I do not want anybody telling me I cannot be with my good friend! On the other hand, if I am allergic to my dog, perhaps he should stay outside most of the time. I am amazed that some patients are highly allergic to cats and let the cat sleep in the bedroom! Therefore, while encouraging avoidance of triggers, use some sensitivity to patients as well as common sense.

Objective Monitoring with Peak Flow Meters
Objective monitoring of lung function by use of peak flow meters is another important component of optimal management for patients with moderate and severe asthma. Analogous to home blood pressure monitoring and home blood glucose monitoring, having an objective measure of...
lung function is quite valuable. The peak expiratory flow rate (PEFR) is easily measured at home by use of peak flow meters (e.g., Assess, Mini-Wright). Correct technique in using peak flow meters is discussed in your required reading, and I'll demonstrate use later in this lecture. PEFR should be recorded every morning and evening.

Colored zones are used to help patients and clinicians in assessment. The “green zone” is defined as 80-100 percent of predicted or “personal best” (doing well). The “yellow zone” is 50-80 percent (call physician for adjustment of long term preventive medication). Finally, the “red zone” is less than 50 percent (call physician immediately, start crisis plan, or go to ED if two puffs of a beta agonist do not bring you back to yellow zone). The predicted value is based on age height and gender and is easily obtained from the product package information, the NIH Expert Panel Report, or journal articles.

In our clinic, we use colored stickers placed directly on the peak flow meter to show the zones. Patients generally love their stickers (there is a kid in each one of us), and they love the enhanced control over their condition that the peak flow meter gives them. Health professionals appreciate having an objective measure when patients call and say they are having an exacerbation (i.e., it helps in decisions regarding more therapy at home or come to the ED). In addition, it is very helpful to have a record of PEFR to review since the last clinic visit. As I demonstrate correct use now, note that I will fill my lungs slowly to full capacity, make a tight seal with my lips around the mouthpiece, and then exhale as fast as I can and with maximum effort—hence peak expiratory flow rate.

Patient Education and Partnership between Health Professional and Patient

Detailed information on several aspects of patient education will be covered in a subsequent lecture. I want to stress here that patient education is an integral part of optimal management and improved clinical outcomes. Simply sharing lots of information is clearly inadequate. A “partnership” must be established between the patient and the health professional. That does not mean exclusively the physician-patient relationship! It means the pharmacist and the patient also have a “partnership.” What do we mean by “partnership”? After demonstrating a caring attitude and good listening skills, involving the patient in decision making regarding long term care is important. Compliance is enhanced in many patients if they feel a greater sense of control. Teaching the patient self-management techniques is part of the partnership as well as letting the patient know that you are easily accessible.

In educating asthmatics, I always start with the principle that asthma symptoms are preventable. In the words of the NIH patient education booklet that we give our clinic patients—Your Asthma Can Be Controlled: Expect Nothing Less! Stressing this concept repeatedly is vital to successful patient education and improved clinical outcomes.

Pharmacologic Therapy

Because asthma is primarily an inflammatory condition, NIH guidelines stress the use of inhaled anti-inflammatory agents in moderate and severe asthmatics(1,2). For children, the initial agent of choice is cromolyn, and for adults the initial choice for most patients is an inhaled corticosteroid (ICS). If a child does not respond adequately to cromolyn, ICS are indicated. Note in your syllabus (Figure 1) the emphasis on these agents in the International Consensus Report’s “Step Care Management” recommendations(2).

Let me stress that there is a wide dosage range for ICS, and that some patients are labeled as “failures” on ICS therapy when the prescribed dose was well below the dose needed. In our lecture on patient education, we shall discuss other reasons for “failures” including poor compliance and poor inhalation technique. Please remember this point—the cornerstone of optimal long term management for moderate to severe asthma is an inhaled anti-inflammatory agent. Many patients are still given bronchodilators only and suffering because of it! I want you to intervene when you see this in moderate and severe asthmatics—quote the NIH Guidelines, and have the therapy changed.

A relatively new anti-inflammatory aerosol is nedocromil, which is similar in mechanism and efficacy to cromolyn. Note in the “Step Care” guidelines (Figure 1) nedocromil is an alternative to ICS in moderate adult asthmatics. While it is not as efficacious as ICS, it is a helpful preventive agent, and for physicians who are unjustifiably hesitant about using ICS, a therapeutic trial is warranted. As with cromolyn in children, if nedocromil therapy is inadequate, ICS should be initiated.

Although the primary long term therapy for excellent asthma control is an inhaled anti-inflammatory agent, all asthmatics also need a short acting inhaled beta2 agonist (e.g., albuterol). These agents are essential for “as needed” use to give rapid relief of symptoms and are the agents of choice for exercise-induced asthma (i.e., exercise for < three hours). Optimized inhaled anti-inflammatory therapy will give such excellent asthma control in many patients that “as needed” use of short acting inhaled beta agonists will be infrequent. How often short acting inhaled beta agonists are needed is a marker of adequacy of anti-inflammatory therapy. If these agents are regularly required to relieve symptoms four times daily or more often, anti-inflammatory therapy needs reassessment. Debates about concerns with prescribing regularly scheduled inhaled beta agonists will be discussed in a subsequent lecture.

Beyond the core therapy of an inhaled anti-inflammatory agent and a short acting inhaled beta2 agonist, giving patients an emergency supply of oral corticosteroid (e.g., prednisone) is important. Early initiation of oral corticosteroids in acute exacerbations at home is well documented to help prevent further escalation of the disease in many patients and often results in reduced ED visits and hospitalizations(3,4). In our asthma clinic, we have found a crisis supply of prednisone 40 mg daily for three days is remarkably helpful in reducing ER visits(5). Use of crisis prednisone at home is warranted, for example, when the PEFR is less than 50 percent of personal best and symptoms and PEFR are not improved after use of a short acting inhaled beta2 agonist.

Other important considerations for long term management include treatment of rhinitis, sinusitis, and gastroesophageal reflux. Each of these problems may trigger asthma in some patients, and they must be addressed for optimal outcomes(1,2).

What about other asthma medications like theophylline and oral beta agonists? These agents may be helpful in some patients, but are now considered adjunctive therapy. Furthermore, with the advent of long acting inhaled beta2...
Figure I. Chronic management of asthma: stepwise approach to asthma therapy. (Reprinted from reference 2.)

**Step-up:** Progression to the next higher step is indicated when control cannot be achieved at the current step and there is assurance that medication is used correctly. If PEFR < 60% predicted or personal best, consider a burst of oral corticosteroids and then proceed.

**Step-down:** Reduction in therapy is considered when the outcome for therapy has been achieved and sustained for several weeks or even months at the current step. Reduction in therapy is also needed to identify the minimum therapy required to maintain control.

**Outcome: Control of Asthma**
- Minimal (ideally no) chronic symptoms, including nocturnal symptoms
- Minimal (infrequent) episodes
- No emergency visits
- Minimal need for prn beta-agonist
- No limitations on activities
- PEFR circadian variation < 20%
- (Near) normal PEFR
- Minimal (or no) adverse effects from medicine
- Least adverse side effects from medicine

**Outcome: Best Possible Results**
- Least symptoms
- Least need for prn beta-agonist
- Least limitation of activity
- Least PEFR circadian variation
- Best PEFR

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**Therapy**

**Therapy**
- **Inhaled anti-inflammatory daily**
  - Initially: Inhaled corticosteroid 200–500μg or cromolyn or nedocromil (Children begin with a trial of cromolyn)
  - If necessary: inhaled corticosteroid 400–750μg (Alternatively, particularly for nocturnal symptoms, proceed to Step 3 with additional long-acting bronchodilator)
  - Short-acting inhaled beta-agonist prn, not to exceed 3–4 times a day

**Therapy**
- Inhaled corticosteroids daily 800–1000μg (or 1000μg under specialist’s supervision) and
- Sustained release theophylline, oral beta-agonist, and short-acting inhaled beta-agonist, not to exceed 3–4 times a day
- Short-acting inhaled beta-agonist prn, not to exceed 3–4 times a day

**Therapy**
- Inhaled corticosteroids 800–1000μg daily (>1000μg under specialist’s supervision)
- Sustained release theophylline and/or oral beta-agonist, or long-acting inhaled beta-agonist, especially for nocturnal symptoms with or without
- Short-acting inhaled beta-agonist once a day may consider inhaled anticholinergic
- Oral corticosteroids (alternate day or single daily dose)
- Short-acting inhaled beta-agonist prn, up to 3–4 times a day

**Step Down**
- Once control is reached at any step and sustained, a step down reduction in therapy may be carefully considered and is needed to identify the minimum therapy required to maintain control.
- Advise patients of signs of worsening asthma and actions to control it.

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**Clinical Features Pretreatment**
- Intermittent, brief symptoms < 1–2 times a week
- Nocturnal asthma symptoms < 1–2 times a month
- Asymptomatic between exacerbations
- PEFR > 80%, predicted

**Clinical Feature Pretreatment**
- Exacerbations > 1–2 times a week
- Exacerbations may affect activity and sleep
- Nocturnal asthma symptoms > 2 times a month
- Chronic symptoms requiring short-acting beta-agonist daily
- PEFR or FEV₁ > 60–80% predicted
- Variability 20–30%

**Clinical Feature Pretreatment**
- Frequent exacerbations
- Continuous symptoms
- Frequent nocturnal asthma symptoms
- Physical activities limited by asthma
- PEFR or FEV₁ < 60 predicted
- Variability > 30%

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*All therapy must include patient education about prevention (including environmental control where appropriate) as well as control of symptoms.*

*One or more features may be present to be assigned a grade of severity; an individual should usually be assigned to the most severe grade in which any feature occurs.*

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*Figure I. Chronic management of asthma: stepwise approach to asthma therapy. (Reprinted from reference 2.)*
agonists like salmeterol (which we shall discuss in a moment), the role of sustained-release theophylline or sustained-release oral beta agonists can now seriously be questioned in many asthmas. Why is this true? Oral agents generally have far more side effects and less efficacy than inhaled agents. As will be discussed in a later lecture, safety concerns are especially true for theophylline when it is not properly dosed and monitored.

SELECTED CLINICAL TRIALS DEMONSTRATING IMPROVED OUTCOMES

Now that we have discussed the NIH Guidelines, let’s look at some clinical trials demonstrating the value of applying these therapeutic principles. Mayo et al.(3) conducted a study in adult patients in New York City with frequent ED visits and hospitalizations. In an effort to reduce acute care management in these patients, the investigators provided the following interventions: detailed patient education, drug therapy emphasis with aggressive ICS therapy via a spacer device, emergency supply of prednisone, PEFR monitoring at home, and easy access to the clinic. These interventions resulted in a three-fold reduction in readmission rate to the hospital.

Mayo et al.(3) had primarily Hispanics in their clinic, as well as some African Americans and Caucasians. My colleagues and I initiated a similar clinic in Memphis recently in order to improve clinical outcomes, but have an exclusively African American population. In addition, our clinic is doctor of pharmacy initiated and managed, while working closely with our colleagues in pulmonary medicine. At this point we have analyzed our data after having followed the patients for one year(5). We are elated that ED visits have been reduced by 90 percent, and we are confident that quality of life is also improving at a minimum because of less illness requiring ED visits. Our management, including intensive patient education, is consistent with NIH Guidelines(1,2) and the Mayo et al. paper(3). A recent University of Tennessee graduate conducted a similar trial in his post-PharmD residency and also found a marked decrease in ED visits(6).

Two California groups have recently shown improved outcomes by using similar approaches in asthmatics in a large managed care organization (Kaiser Permanente) Im(7) has described excellent effectiveness of an asthma clinic managed by an ambulatory care pharmacist. In the initial year of her program, a 66 percent reduction in ED visits was achieved as well as a 50 percent reduction in hospitalizations. Zeiger and associates(8) also have demonstrated that application of the principles in the NIH Guidelines improve outcomes. In this study, referral to allergists from generalists reduced ED visits(8).

Let me emphasize again that improving outcomes involves not only proper drug selection and tailored dosing, but also careful, repetitive patient education. In each of the trials we have just mentioned, whether pharmacist, MD, or nurse, patient education was critically important. Absolutely essential components of education include demonstrations of MDA/spacer and peak flow meter use and subsequent observation of the patient on each encounter. Clear distinction between “preventers” and “quick relievers” is also imperative. These points, along with demonstrations and case studies, will be discussed in detail over the next few days of lecture.

ROLE OF SALMETEROL IN LONGTERM MANAGEMENT

Since the release of the NIH Guidelines, salmeterol has become available. The exact place of this 12-hour duration inhaled beta2 agonist is still being determined through continued research. Clearly, patients who are receiving adequate inhaled anti-inflammatory therapy and have quick relief of symptoms with infrequent use of short acting inhaled beta2 agonists do not need salmeterol. On the other hand, patients who frequently require “as needed” short acting agents despite adequate anti-inflammatory therapy can benefit from salmeterol therapy(9). Further, the addition of salmeterol therapy to low and moderate doses of ICS has eliminated the need for further increases in ICS dose in initial short term trials(10,11).

Perhaps the best known impact of salmeterol is its excellent efficacy in nocturnal asthma(12). The 12-hour plus duration of action has been shown to result in improved morning PEFR and improved sleep quality. Salmeterol is also a good choice for the prevention of asthma in patients who exercise for periods greater than three to four hours, because it offers protection over 12 hours versus < four hours protection with short acting inhaled beta2 agonists(13).

Salmeterol costs more than short acting inhaled beta agonists. The primary cost issue in long term management, however, concerns clinical outcomes and not unit cost of a drug. If anti-inflammatory therapy and infrequent use of short acting beta agonists is providing excellent outcomes, salmeterol would needlessly increase the cost of care. On the other hand, for a large number of asthmatics, salmeterol therapy in combination with inhaled anti-inflammatory agents is extremely cost effective because of improved outcomes. Later in this lecture series on asthma, we shall discuss more specifics on the costs of ED visits and hospitalizations as well as the cost of medications and the human “costs” associated with this condition.

CONCLUSION

By applying NIH Guidelines and other current literature, you can improve clinical outcomes in asthmatics. Pharmacists can help reduce ED visits and hospitalizations, and we can reduce the cost of care and improve quality of life. Most importantly we can reduce human suffering. I urge you to establish partnerships with patients and physicians. My great hope is that you will share your knowledge and skill with other health professionals regarding optimal long term management of asthma and that you will provide care for these patients as if you were providing care for your best friend or a family member.

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References

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